COMPARING A NOVEL SOLUBILIZED BENZOYL PEROXIDE GEL WITH BENZOYL PEROXIDE/CLINDAMYCIN: FINAL DATA FROM A MULTICENTER, INVESTIGATOR-BLIND, RANDOMIZED STUDY

Leon Kircik, MD
Physicians Skin Care PLLC
Louisville, KY

Lawrence Green, MD
George Washington University
Washington, DC

Diane Thiboutot, MD
Penn State University College of Medicine
Hershey, PA

Emil Tanghetti, MD
Center for Dermatology and Laser Surgery
Sacramento, CA

David Wilson, MD
Education and Research Foundation
Lynchburg, VA

Sunil Dhawan, MD
Center for Dermatology, Cosmetic and Laser Surgery
Fremont, CA

INTRODUCTION

A novel solubilized 5% BPO gel has recently become available as a treatment for acne vulgaris—both as a stand-alone product[1] and as part of a 3-step acne system[2] (in conjunction with a proprietary cleanser and toner containing 2% salicylic acid). In other formulations of BPO, the bioavailability and follicular penetration of BPO can be suboptimal because the molecule is only poorly soluble and can exist as macrocrystals whose diameters may exceed those of hair follicles. In contrast, the solubilized BPO formulation aims to maintain the BPO in solution in order to promote greater BPO bioavailability and greater penetration of BPO into the follicles.

We have compared the efficacy and tolerability of the solubilized 5% BPO formulation with those of a leading 5% BPO/clindamycin prescription product in a multicenter investigator-blinded study. An initial set of 4-week data from this study has been presented previously.[3] Additional patients have subsequently been enrolled into the study and the period of treatment has been extended to 12 weeks. Overall results from both parts of the study are reported here.

METHODS

Study design

- Multicenter, investigator-blind, randomized, split-face study

Key inclusion criteria

- Moderate facial acne vulgaris (25-100 non-inflammatory lesions, 25-100 inflammatory lesions, up to 2 nodulocystic lesions)
- 11-45 years of age
- Willing to refrain from excessive exposure to the sun and the use of tanning booths
- Willing to refrain from facial use of non-study acne medications, moisturizers, sunscreens, fragrances, aftershaves, and make-up (however, oil-free non-comedogenic make-up, mascara, eyeshadow, and lipstick were allowed)

Key exclusion criteria

- Allergy to benzoyl peroxide, clindamycin, lincomycin, salicylic acid, sunscreens or other ingredients in the study products
- Facial cosmetic procedure in the preceding 6 months
- Papulopustular rosacea and other skin diseases on the face (other than acne) that could interfere with study evaluations
- Facial sunburn at the baseline visit
- Males with a beard or sideburn that could interfere with study evaluations
- Uncontrolled systemic disease or infection with human immunodeficiency virus
- History of regional enteritis, ulcerative colitis, or antibiotic-associated colitis
- Concurrent facial use of other medicated products
- Participation in an investigational study in preceding 30 days

Washout periods

- 1 week for medicated facial cleansers
- 2 weeks for topical alpha-hydroxy acids, anti-acne medications, topical retinoids, topical and systemic antibiotics, topical and systemic steroids
- 3 months for estrogens/birth control pills (unless use had been stable for at least 3 months)
- 6 months for systemic retinoids

Treatment regimen

- Patients were randomly assigned to apply one of the following to one side of their face and the other to the contralateral side of their face, twice daily for 4 or 12 weeks:
  - Solubilized 5% BPO gel
  - 5% BPO/1% clindamycin combination product (gel product packaged in a pump).
- Before applying either product, patients were required to wash their face using a gentle cleanser (provided).
- Patients were instructed to avoid applying the test products around the lips and eyes and were allowed to use a non-comedogenic moisturizer with sunscreen (of at least SPF 15) as necessary during the study.

TABLE 1 Scales used to evaluate tolerability parameters.

Scale	Erythema	Dryness	Peeling	Stinging/burning	Itching
0	None – no erythema present (may be minor discoloration)	None – no dryness present	None – no peeling present	None – no stinging/burning	None – no itching
1	Mild – light pink, noticeable	Mild – slight but definite roughness	Mild – slight peeling	Mild – light warm, tingling sensation, not really bothersome	Mild – occasional, slight itching
2	Moderate – pink-red, easily noticeable	Moderate – moderate roughness	Moderate – definitely noticeable peeling	Moderate – definite warmth, tingling/stinging sensation that is somewhat bothersome	Moderate – constant or intermittent itching that is somewhat bothersome
3	Severe – deep or bright red, may be warm to the touch	Severe – marked roughness	Severe – extensive peeling	Severe – hot tingling/stinging sensation which is disturbing normal activity	Severe – bothersome itching which is disturbing normal activity

Outcome measures

- Non-inflammatory lesion count (open comedones plus closed comedones)
- Inflammatory lesion count (papules plus pustules plus nodules)
- Patient satisfaction with the improvement in their acne (rated as very satisfied, satisfied, somewhat satisfied, indifferent, or dissatisfied)
- Erythema, dryness, peeling, stinging/burning, and itching (Table 1)

Statistical analyses

- Between-group differences in lesion count and mean scores for erythema, dryness, peeling, stinging/burning, and itching were compared using a paired t-test or Wilcoxon signed rank test.
- A P value of ≤.05 was considered statistically significant.

RESULTS

Patients

- A total of 65 patients enrolled:
  - 23 to receive 4 weeks of treatment (of whom, 100% completed)
  - 42 to receive 12 weeks of treatment (of whom, 37 (88%) completed).
- Premature discontinuations from the study were due to non-compliance (2), burning sensation and erythema (1), voluntary withdrawal (1), and loss to follow-up (1).
- The patients had a mean age of 19 years and 54% were female.
- They were predominantly:
  - Caucasian (71% Caucasian, 6% Caucasian Hispanic/Latino, 14% Black, 3% Asian, 6% other)
  - Fitzpatrick skin type III (13% I, 25% II, 39% III, 8% IV, 5% V, 10% VI).

Efficacy

- The solubilized BPO gel resulted in a significantly greater reduction in non-inflammatory lesion count than BPO/clindamycin at weeks 1, 2, 3, 4, and 12 (P≤.05, Figure 1).
- At week 12, the non-inflammatory lesion count (Figure 1) was reduced by a mean of:
  - 57% with the solubilized BPO gel (P≤.05 versus BPO/clindamycin)
  - 46% with BPO/clindamycin.
- Both groups showed comparable reductions in the inflammatory lesion count at all timepoints (Figure 2).
- At week 12, the inflammatory lesion count (Figure 2) was reduced by a mean of:
  - 63% with the solubilized BPO gel
  - 64% with BPO/clindamycin.

Patient satisfaction

- Patient satisfaction with the improvement in their acne was comparable in both groups at all timepoints (Figure 3).

Tolerability

- Mean levels of erythema, dryness, peeling, stinging/burning, and itching were less than mild in both groups at all timepoints (Figures 4-8).
- Although the mean levels of these parameters were significantly higher with the solubilized BPO gel than with BPO/clindamycin in the first 3 or 4 weeks of treatment, these differences were transient and were likely not clinically significant in the majority of patients—as evidenced by the fact that there was no significant between-group difference in mean patient satisfaction score at any timepoint.
- One patient discontinued prematurely due to adverse events (burning on the side of the face treated with the BPO/clindamycin product, and erythema on both sides of the face).
- In addition, another patient discontinued applying the solubilized 5% BPO gel to one side of their face (due to a burning sensation on their temple) but continued applying BPO/clindamycin to the other side of their face.

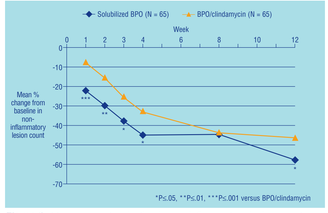

Figure 1. Mean percent reduction in non-inflammatory lesion count.

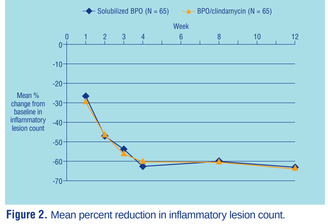

Figure 2. Mean percent reduction in inflammatory lesion count.

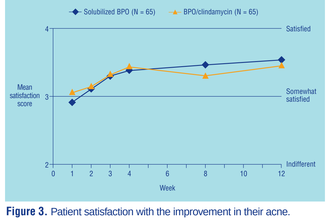

Figure 3. Patient satisfaction with the improvement in their acne.

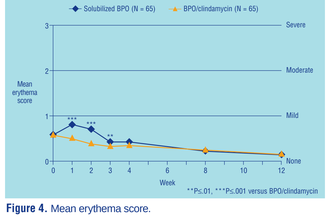

Figure 4. Mean erythema score.

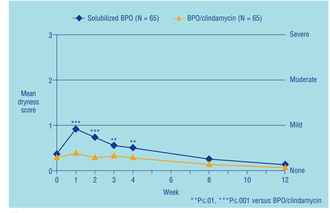

Figure 5. Mean dryness score.

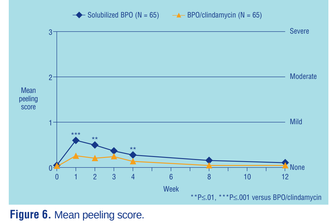

Figure 6. Mean peeling score.

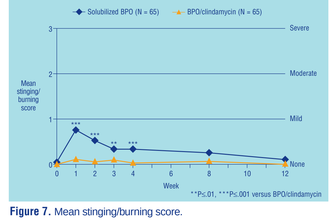

Figure 7. Mean stinging/burning score.

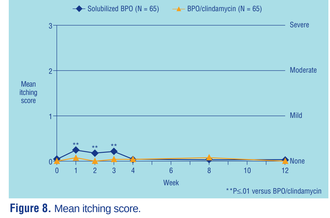

Figure 8. Mean itching score.

CONCLUSIONS

In this study, twice-daily monotherapy with the solubilized 5% BPO gel resulted in significantly greater reductions in non-inflammatory lesion count compared with twice-daily therapy with a 5% BPO/clindamycin combination product. Levels of patient satisfaction, and reductions in inflammatory lesion count, were comparable in both groups. The significantly greater reduction in non-inflammatory lesion count with the solubilized BPO gel is likely attributable to enhanced follicular penetration of BPO. It is also possible that the unique solvent technology used in the BPO formulation could play a role.

The solubilized BPO gel has two advantages of considerable clinical importance. First, significantly greater reductions in non-inflammatory lesion count may be evident after only 1 week of treatment (and speed of improvement is very important to patients). Second, the clinical advantages of the solubilized 5% BPO gel in achieving a comparable reduction in inflammatory lesion count and a significantly greater reduction in non-inflammatory lesion count are achieved in the absence of an antibiotic.

REFERENCES

1. Introducing SoluCLENZ Rx Gel™. Obagi Medical Products web site. http://www.obagi.com/article/forpatients/obagisoluclenzrx/soluclenz.html. Accessed December 2, 2008.
2. CLENZIderm M.D. - Product Detail. Obagi Medical Products web site. http://www.obagi.com/article/forpatients/obagiclenzidermmd/products/products.html. Accessed December 1, 2008.
3. Tanghetti E, Kircik L, Wilson D, Dhawan S. Comparison of a novel solubilized benzoyl peroxide gel with benzoyl peroxide/clindamycin: A multicenter, investigator-blind, randomized study. Poster #123 presented at the 66th Annual Meeting of the American Academy of Dermatology, February 1-5, 2008, San Antonio, TX. http://www.obagi.com/documents/N0A%20010A%20Poster%20FINAL.pdf. Accessed December 5, 2008.

DISCLOSURES

Supported by OMP, Inc.