A COMPARISON OF A NOVEL BENZOYL PEROXIDE SYSTEM WITH A COMBINATION BENZOYL PEROXIDE AND CLINDAMYCIN PRODUCT: A 2-WEEK SPLIT-FACE STUDY OF EFFECTIVENESS AND TOLERABILITY

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INTRODUCTION

Benzoyl peroxide (BPO) has both bactericidal activity against *Propionibacterium acnes* and comedolytic activity, and therefore offers efficacy against both inflammatory and non-inflammatory acne lesions.[1,2] However, the bioavailability of BPO in commercially successful formulations is generally suboptimal because BPO is poorly soluble and because some vehicles hinder the ability of BPO to enter the follicles and so reach areas where *P. acnes* proliferate. If the bioavailability and penetration of BPO could be enhanced, it is possible that the clinical efficacy of BPO could also be enhanced.

A novel solubilized BPO formulation has recently been developed that offers high bioavailability of BPO in a gel that can enter the follicles.[3] The results of a split-face randomized study with this solubilized 5% BPO gel have shown that it offers greater bactericidal activity against *P. acnes* in the follicles and on the skin surface than either a generic 5% BPO formulation or a combination 5% BPO/clindamycin product.[4]

Another split-face randomized study has now been performed to compare the clinical efficacy and tolerability of this solubilized BPO gel (plus toner) with that of a commercially available BPO/clindamycin product.

METHODS

Study design

- Investigator-blind, randomized, split-face study

Key inclusion criteria

- Mild to moderate facial acne:
  - 17-40 inflammatory lesions
  - 10-100 non-inflammatory lesions
  - Fairly even distribution of lesions on face
- 12-40 years of age
- Willing to refrain from sun exposure and from using non-study acne medications during study

Key exclusion criteria

- Papulopustular rosacea and other skin diseases on the face (other than acne)
- Facial suntan or sunburn
- Allergy to benzoyl peroxide or sunscreens
- Beard if would interfere with the study evaluations
- Uncontrolled systemic disease or insulin-dependent diabetes
- Concurrent use of other medicated products or any new cosmetics on the face
- Immunological disorders
- Pregnancy or lactation

Washout periods

- 1 week for medicated facial cleansers
- 2 weeks for topical AHAs and anti-acne medications (except topical retinoids and antibiotics)
- 4 weeks for topical retinoids, topical and systemic antibiotics, topical and systemic steroids, investigational drugs, and any drug applied to the face as part of a clinical trial
- 12 weeks for estrogen/birth control pills if used for less than 3 months preceding study start (or 6-month washout if indicated for acne treatment and used for less than 6 months preceding study start)
- 1 year for systemic retinoids

Treatment regimen

- All patients applied one of the following treatment regimens to one side of their face and the other regimen to the other side of their face twice daily for 2 weeks:
  - Solubilized 5% BPO gel plus toner
  - Commercially available BPO/clindamycin combination product.
- Facial side was determined by random assignment.
- The toner (containing 2% salicylic acid) was intended to enhance the anti-acne efficacy and keratolytic actions of BPO.
- Both sides of the face were washed using the same gentle cleanser before the test products were applied.
- The products were dispensed from pumps or pads and the patients were given comprehensive instructions and training on how to apply them. The first application was performed under supervision and the patients returned the next day for additional training and to ensure compliance.
- They were instructed to:
  - Avoid using any other medicated formulations on their face
  - Avoid prolonged UV exposure (and, if not possible, to use moisturizer/sunscreen on the treatment area)
  - Avoid facial washing for at least 6 hours after each treatment.
- Patients were allowed to continue using their regular non-medicated make-up providing that, at weeks 1 and 2, they did not apply them until *after* their office evaluation visits.

Outcome measures

- The investigator evaluated patients at baseline, week 1, and week 2 in terms of:
  - Inflammatory lesion count
  - Non-inflammatory lesion count
  - Acne Global Assessment grade (Table 1)
  - Erythema (Table 1)
  - Dryness (Table 1).
- The patients evaluated itching and stinging/burning (Table 1).

TABLE 1 Scales used for outcome measures.

Score	Acne Global Assessment	Erythema	Dryness	Itching	Stinging/burning
0	**None** Normal, clear skin with no evidence of acne vulgaris	**None** No erythema present (may be minor discoloration)	**None** No dryness	**None** No itching	**None** No stinging/ burning
1	**Almost Clear** Skin almost clear: rare non-inflammatory lesions present, with rare non-inflamed papules (papules must be resolving and may be hyperpigmented, though not pink)	**Mild** Light pink, noticeable	**Mild** Slight but definite roughness	**Mild** Occasional, slight itching	**Mild** Light warm, tingling sensation, not really bothersome
2	**Mild** Some non-inflammatory lesions present, with few inflammatory lesions (papules/pustules only; no nodulocystic lesions)	**Moderate** Pink-red, easily noticeable	**Moderate** Moderate roughness	**Moderate** Constant or intermittent itching that is somewhat bothersome	**Moderate** Definite warmth, tingling/stinging sensation that is somewhat bothersome
3	**Moderate** Non-inflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/ pustules, may or may not be one small nodulocystic lesion	**Severe** Deep or bright red, may be warm to the touch	**Severe** Marked roughness	**Severe** Bothersome itching which is disturbing normal activity	**Severe** Hot tingling/ stinging sensation which is disturbing normal activity
4	**Severe** Inflammatory lesions are more apparent: many comedones and papules/pustules, may or may not be a few nodulocystic lesions				
5	**Very Severe** Highly inflammatory lesions predominate: variable number of comedones, many papules/ pustules and/or nodulocystic lesions				

RESULTS

Patients

- Of 34 patients enrolled, 27 (79%) completed the study and were assessed for effectiveness at 2 weeks.
- Three subjects discontinued due to mild dryness, erythema, swelling, and itching on the cheeks, and 4 discontinued due to non-compliance/withdrawal of consent.
- The patients had a mean age of 19 years (range, 13-38 years).
- They were predominantly:
  - Female (56%)
  - White (68% white, 29% Black/African American, 3% Asian)
  - Fitzpatrick skin type III (12% II, 53% III, 6% IV, 29% V).
- At baseline, patients had a:
  - Mean of 25 inflammatory lesions
  - Mean of 41 non-inflammatory lesions
  - Acne Global Assessment grade of either moderate or severe (74% and 26% of each group, respectively).

Efficacy

- The solubilized BPO regimen resulted in greater—and more rapid—reductions in lesion counts than the BPO/clindamycin regimen (Figures 1 and 2), a mean of:
  - 23% versus 12% reduction in inflammatory lesion count at week 1
  - 52% versus 50% reduction in inflammatory lesion count at week 2
  - 13% versus 5% reduction in non-inflammatory lesion count at week 1
  - 34% versus 21% reduction in non-inflammatory lesion count at week 2.
- At week 2, the proportion of patients who had at least a 1-grade improvement in Acne Global Assessment (eg, from severe to moderate or from moderate to mild) was:
  - 89% with the solubilized BPO regimen
  - 85% with the BPO/clindamycin regimen.
- The proportion of patients whose Acne Global Assessment grades had improved (from their baseline levels of moderate or severe) to mild, almost clear, or clear (Figure 3) was:
  - 39% vs. 29% at week 1 (for solubilized BPO regimen vs. BPO/clindamycin)
  - 81% vs. 78% at week 2.

Tolerability

- Overall, 4 of the 34 patients reported adverse events typical of BPO-containing products (mild burning, dryness, stinging, erythema, swelling, and itching). One of these subjects also reported a rash on the cheek.
- The mean scores for erythema, dryness, itching, and stinging/burning were mild or less than mild throughout the study (Figures 4-7).
- No serious adverse events were reported.

FIGURE 1 Reduction in inflammatory lesion count.

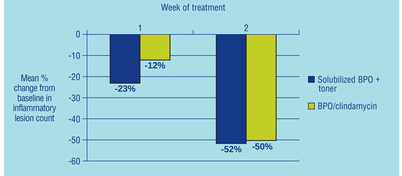


FIGURE 2 Reduction in non-inflammatory lesion count.

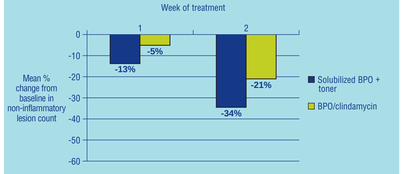


FIGURE 3 Patients whose Acne Global Assessment grade had improved to mild, almost clear, or clear (from baseline levels of moderate or severe).

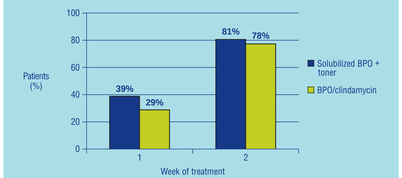


FIGURE 4 Mean erythema score.

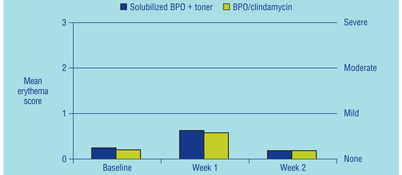


FIGURE 5 Mean dryness score.

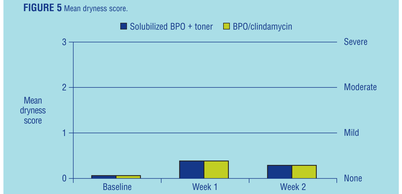


FIGURE 6 Mean itching score.

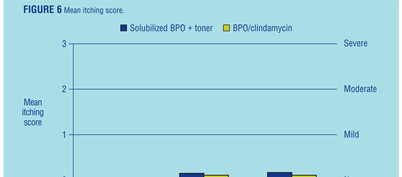
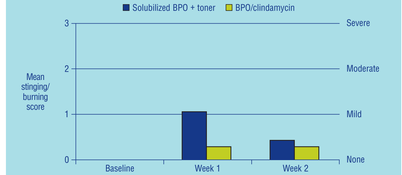


FIGURE 7 Mean stinging/burning score.



CONCLUSIONS

The regimen of a novel solubilized 5% BPO gel plus a 2% salicylic acid-based toner achieved a faster reduction in acne lesions than the BPO/clindamycin combination product. After 2 weeks of treatment, the solubilized BPO regimen had achieved a greater reduction in non-inflammatory lesion count than BPO/clindamycin and a comparable reduction in inflammatory lesion count. The reduction in inflammatory lesion count observed with the solubilized BPO regimen in the absence of a traditional antibiotic is potentially of considerable clinical importance.

REFERENCES

1. Belknap BS. Treatment of acne with 5% benzoyl peroxide gel or 0.05% retinoic acid cream. *Cutis* 1979;23:856-9.
2. 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(1 suppl):S1-S37.
3. Spellman MC, Ramirez J. A comparison of patterns of deposition of two formulations of benzoyl peroxide on the skin and in the follicular ostia as visualized by scanning electron microscopy. Poster presented at the 65th Annual Meeting of the American Academy of Dermatology, February 2-6, 2007, Washington, DC.
4. Erianne J, Prince DL, Ramirez J, Wilson D, Zeichner J. The pharmacologic science of a novel benzoyl peroxide formulation and the implications for clinical effects. Poster presented at the 25th Anniversary Fall Clinical Dermatology® Conference, October 6-9, 2006, Las Vegas, NV.

DISCLOSURES

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