META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS USING BENZOYL PEROXIDE AND CLINDAMYCIN TOPICAL TREATMENTS IN ACNE

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ABSTRACT

Benzoyl peroxide (BPO) plays an important role in topical antimicrobial acne treatment. We sought to evaluate the efficacy of a recently developed formulation of solubilized 5% BPO in a regimen that sometimes included (±) 2% salicylic acid compared with other products containing 5% BPO, 1%-1.2% clindamycin (CL), or combination BPO/CL. A meta-analysis following the Cochrane collaboration guidelines in accordance with the PRISMA statement was conducted. Data sources included the PubMed database from 1987 to the present, FDA summaries for the basis of drug approval, and posters and unpublished statistical analyses of studies where available. We identified randomized controlled trials that treated subjects with 5% BPO, 1%-1.2% clindamycin, or a combination BPO/clindamycin product and which included endpoints of actual reduction and/or percent reduction of inflammatory and/or non-inflammatory lesions at weeks 2-4 and/or weeks 10-12. We identified 124 randomized controlled trials under our search criteria, of which 23 met all inclusion and exclusion criteria and were deemed valid to include in the meta-analysis. These studies involved 210 subjects receiving 5% solubilized BPO ± salicylic acid (145 received salicylic acid and 65 did not), 824 subjects receiving 5% BPO, 3,143 subjects receiving 1%-1.2% clindamycin, 1,923 subjects receiving combination BPO/clindamycin, and 1,308 subjects receiving placebo. At weeks 2-4, the percent reduction in both inflammatory lesion count and non-inflammatory lesion count was statistically greater with 5% solubilized BPO ± salicylic acid than any of the other treatments, with non-overlapping 95% confidence intervals. Weighted mean reductions in inflammatory lesion count were 55.2% with solubilized BPO ± salicylic acid, 33.4% with BPO, 21.5% with clindamycin, 40.7% with BPO/clindamycin combination, and 7.3% with placebo; weighted mean reductions in non-inflammatory lesion count were 42.7% with solubilized BPO ± salicylic acid, 19.1% with BPO, 10.0% with clindamycin, 26.2% with BPO/clindamycin combination, and 6.7% with placebo. At weeks 10-12, 5% solubilized BPO ± salicylic acid had similar efficacy to BPO/clindamycin combination products with overlapping confidence intervals. However, there were only two studies with 5% solubilized BPO ± salicylic acid that extended to 10-12 weeks (one involved salicylic acid and one did not). Weighted mean reductions in inflammatory lesion count were 51.8% with solubilized BPO ± salicylic acid, 43.7% with BPO, 45.9% with clindamycin, 55.6% with BPO/clindamycin combination, and 26.8% with placebo; weighted mean reductions in non-inflammatory lesion count were 47.8% with solubilized BPO ± salicylic acid, 30.9% with BPO, 32.6% with clindamycin, 40.3% with BPO/clindamycin combination, and 17.0% with placebo.

We conclude that 5% solubilized BPO ± salicylic acid offers greater efficacy than 5% BPO, 1%-1.2% clindamycin, and combination BPO/clindamycin products in reducing inflammatory and non-inflammatory lesion counts in the early weeks of treatment. This may be attributable to solubilization of the BPO, which may enhance its bioavailability and intrafollicular penetration. 5% solubilized BPO ± salicylic acid is also at least as effective as these products in reducing lesion counts at weeks 10-12.

INTRODUCTION

Acne treatment commonly involves topical products containing BPO, clindamycin, or both. Comparative efficacy has not been established. A solubilized formulation of 5% BPO has been developed which can be used in conjunction with a 2% salicylic acid cleanser and/or a 2% salicylic acid toner. We conducted a meta-analysis to evaluate the efficacy of the solubilized BPO formulation (± 2% salicylic acid) in reducing acne lesion counts in comparison with other 5% BPO products, 1%-1.2% clindamycin, combination BPO/clindamycin products, and placebo.

METHODS

- A meta-analysis was conducted following the Cochrane collaboration guidelines in accordance with the PRISMA statement.
- Studies were identified for potential inclusion in the meta-analysis using:
  - PubMed database from 1987 to the present
  - FDA summaries for the basis of drug approval
  - Posters and unpublished statistical analyses where available.
- Inclusion criteria:
  - Randomized controlled trials using topical anti-acne medication
  - At least one cohort treated with solubilized 5% BPO ± salicylic acid, another 5% BPO formulation as monotherapy, 1%-1.2% clindamycin, or a BPO/clindamycin combination product
  - Efficacy assessed at weeks 2-4 and/or weeks 10-12 by:
    - Inflammatory lesion count and/or percent reduction in inflammatory lesion count
    - Non-inflammatory lesion count and/or percent reduction in non-inflammatory lesion count.
- Exclusion criteria:
  - Single-arm studies
  - Studies examining acne rosacea
  - Studies with a retinoid in all cohorts.

RESULTS

Studies

- Of 124 studies initially identified for potential inclusion, 23 met all inclusion and exclusion criteria (Figure 1) and were included in the analysis.[1-21]
- These 23 studies (Table 1) involved:
  - 210 subjects receiving 5% solubilized BPO ± salicylic acid (145 received salicylic acid and 65 did not)
  - 824 subjects receiving 5% BPO
  - 3,143 subjects receiving 1%-1.2% clindamycin
  - 1,923 subjects receiving combination BPO/clindamycin (5% BPO/1% clindamycin or 2.5% BPO/1.2% clindamycin)
  - 1,308 subjects receiving placebo.

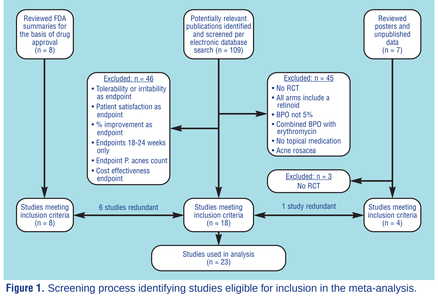

Figure 1. Screening process identifying studies eligible for inclusion in the meta-analysis.

TABLE 1 Summary of trials included in analysis.

Treatment group	Number of studies	Number of subjects
5% solubilized BPO ± salicylic acid	4	210
5% BPO	10	824
1%-1.2% clindamycin	14	3143
Combination BPO/clindamycin (5% BPO/1% clindamycin or 2.5% BPO/1.2% clindamycin)	15	1923
Placebo	9	1308

Efficacy at weeks 2-4

- 5% solubilized BPO ± salicylic acid attained statistically greater percent reductions in inflammatory lesion count and non-inflammatory lesion count than any of the other treatments, with non-overlapping 95% confidence intervals (Figure 2).
- BPO/clindamycin was more efficacious than clindamycin alone and incrementally more efficacious than 5% BPO alone (Figure 2).
- Weighted mean reductions in inflammatory lesion count were:
  - 55.2% with 5% solubilized BPO ± salicylic acid
  - 33.4% with 5% BPO
  - 21.5% with clindamycin
  - 40.7% with BPO/clindamycin combinations
  - 7.3% with placebo.
- Weighted mean reductions in non-inflammatory lesion count were:
  - 42.7% with 5% solubilized BPO ± salicylic acid
  - 19.1% with 5% BPO
  - 10.0% with clindamycin
  - 26.2% with BPO/clindamycin combinations
  - 6.7% with placebo.

Efficacy at weeks 10-12

- 5% solubilized BPO ± salicylic acid attained (Figure 3):
  - Comparable efficacy to BPO/clindamycin combination products, with overlapping confidence intervals.
    (There were, however, only two studies with 5% solubilized BPO ± salicylic acid that had efficacy evaluations at weeks 10-12.)
  - Greater efficacy than 5% BPO and 1%-1.2% clindamycin in reducing the non-inflammatory lesion count.
- BPO/clindamycin had:
  - Greater efficacy than 5% BPO in reducing the inflammatory and non-inflammatory lesion count
  - Greater efficacy than 1%-1.2% clindamycin in reducing the inflammatory lesion count.

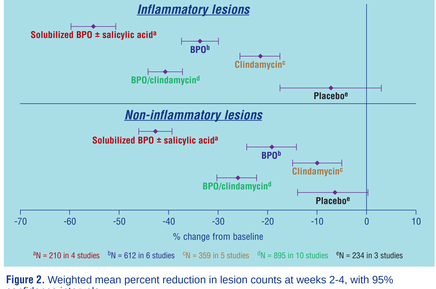

Figure 2. Weighted mean percent reduction in lesion counts at weeks 2-4, with 95% confidence intervals.

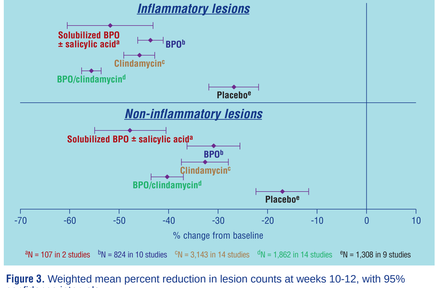

Figure 3. Weighted mean percent reduction in lesion counts at weeks 10-12, with 95% confidence intervals.

- Weighted mean reductions in inflammatory lesion count were:
  - 51.8% with 5% solubilized BPO ± salicylic acid
  - 43.7% with 5% BPO
  - 45.9% with clindamycin
  - 55.6% with BPO/clindamycin combination
  - 26.8% with placebo.
- Weighted mean reductions in non-inflammatory lesion count were:
  - 47.8% with 5% solubilized BPO ± salicylic acid
  - 30.9% with 5% BPO
  - 32.6% with clindamycin
  - 40.3% with BPO/clindamycin combination
  - 17.0% with placebo.

Limitations of the meta-analysis

- Unable to control for methodological differences between studies
- Unable to mitigate any publication biases
- Only 2 studies involving solubilized BPO had data at weeks 10-12
- Tolerability was not considered

CONCLUSIONS

5% solubilized BPO ± salicylic acid offers greater efficacy than 5% BPO, 1%-1.2% clindamycin, and combination BPO/clindamycin products in reducing inflammatory and non-inflammatory lesion counts in the early weeks of treatment (weeks 2-4). This may be attributable to solubilization of the BPO, which may enhance its bioavailability and intrafollicular penetration. 5% solubilized BPO ± salicylic acid is also at least as effective as these products in reducing lesion counts at weeks 10-12.

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DISCLOSURE

Ms Seidler has no conflicts of interest to disclose. Dr Kimball is a consultant for Obagi Medical Products, investigator for Stiefel, consultant for Arcutis, and consultant for Galderma.

SUPPORT

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