# Antibiotic-Resistant *Propionibacterium acnes* Suppressed by a Benzoyl Peroxide Cleanser 6%

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*Adding topical benzoyl peroxide (BPO) to antibiotics can reduce resistant* Propionibacterium acnes *in patients with acne receiving antibiotic therapy. Benzoyl peroxide often is formulated as a wash, but no published data exist regarding BPO wash formulation efficacy in reducing resistant strains of* P acnes. *This 3-week, open-label, single-center study evaluated the effects of BPO cleanser 6% on antibiotic-resistant* P acnes *populations. The study involved 30 healthy adults who were free of acne but had high facial* P acnes *populations (10,000 colonies/cm$^2$ or more) resistant to erythromycin and tetracycline at 8 µg/mL or more and 2 µg/mL or more, respectively. Participants applied BPO cleanser 6% once daily. Quantitative* P acnes *cultures were obtained at baseline and weekly for 3 weeks. At baseline, resistance to erythromycin, tetracycline, doxycycline, minocycline, and clindamycin was present in 100% (30/30), 97% (29/30), 83% (25/30), 63% (19/30), and 100% (25/25) of participants, respectively; high-level resistance for erythromycin and tetracyclines and intermediate to high resistance for clindamycin was present in 100% (30/30), 50% (15/30), 33% (10/30), 27% (8/30), and 52% (13/25) of participants, respectively. Total* P acnes *counts and counts of each resistant strain decreased by approximately 1 log after 1 week of treatment, by at least 1.5 log after 2 weeks of treatment, and by at least 2 log after 3 weeks of treatment, with no differences between resistant and susceptible strains or between highly resistant and low-level resistant strains. Benzoyl peroxide cleanser 6% effectively reduced resistant* P acnes *populations and offers a useful therapy for controlling antibiotic resistance in patients receiving antibiotics.*

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The sensitivity of *Propionibacterium acnes* to antibiotics used to treat acne has changed greatly over the past 20 years. Less sensitive strains of *P acnes* that can result in poor clinical response or resistance are readily found on the skin of patients with acne worldwide.[1-9] The proportion of patients with propionibacteria resistant to one or more antibiotics increased from 34.5% in 1991 to 55.5% in 2000, with the highest resistance rates reported for erythromycin followed by clindamycin.[7] Furthermore, it has been reported that most erythromycin-resistant strains show varying levels of insensitivity to clindamycin.[6]

These findings indicate that clinicians face a growing challenge in caring for patients with acne, including the need to identify and use treatments that will be effective against resistant bacteria and will not promote further resistance. In 2003, a group of worldwide experts concluded that patients

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receiving prolonged antibiotic therapy for acne (≥3 months) also should be treated with topical benzoyl peroxide (BPO) to minimize the emergence of resistant strains.[10]

Prior research has shown that leave-on products containing BPO are effective in suppressing existing insensitive strains as well as preventing their emergence during antibiotic therapy for acne.[11] Other studies showed that topical BPO administered in combination with a topical antibiotic may reduce antibiotic resistance.[9,12-15]

Many different delivery vehicles have been developed for BPO, including washes and leave-on products such as gels and lotions. It is not clear if the formulation affects the impact of BPO on resistant bacteria or to what extent. The leave-on products would be expected to have greater substantivity than washes. However, substantivity has improved in modern BPO wash formulations, and they have been shown to be effective in reducing *P acnes* populations.[10,16] No published studies have compared different wash formulations with each other or with leave-on formulations. The question asked in this study was whether BPO in a wash formulation would be capable of significantly reducing resistant strains of *P acnes*. Thirty participants with strains of *P acnes* resistant to multiple antibiotics were treated once daily for 3 weeks with BPO cleanser 6%. Quantitative cultures demonstrated significant reduction in *P acnes* with sensitive and resistant strains.

## Methods and Materials

This 3-week, open-label, single-center study enrolled 30 healthy adults who were free of acne but had high facial *P acnes* populations. None of the participants used antibiotics during the study or had used antibiotics for a month prior to the study. Participants were treated with a BPO cleanser 6% that was applied to the face once daily by washing the face and massaging the cleanser into the skin for 20 seconds. Washing was performed in a supervised laboratory environment from Monday through Friday and in an unsupervised setting on Saturday and Sunday. A vehicle control group was not included in this study because although a detergent, the vehicle for the BPO wash, can remove surface organisms such as coagulase-negative cocci, it is not capable of removing subsurface *P acnes*. Because the

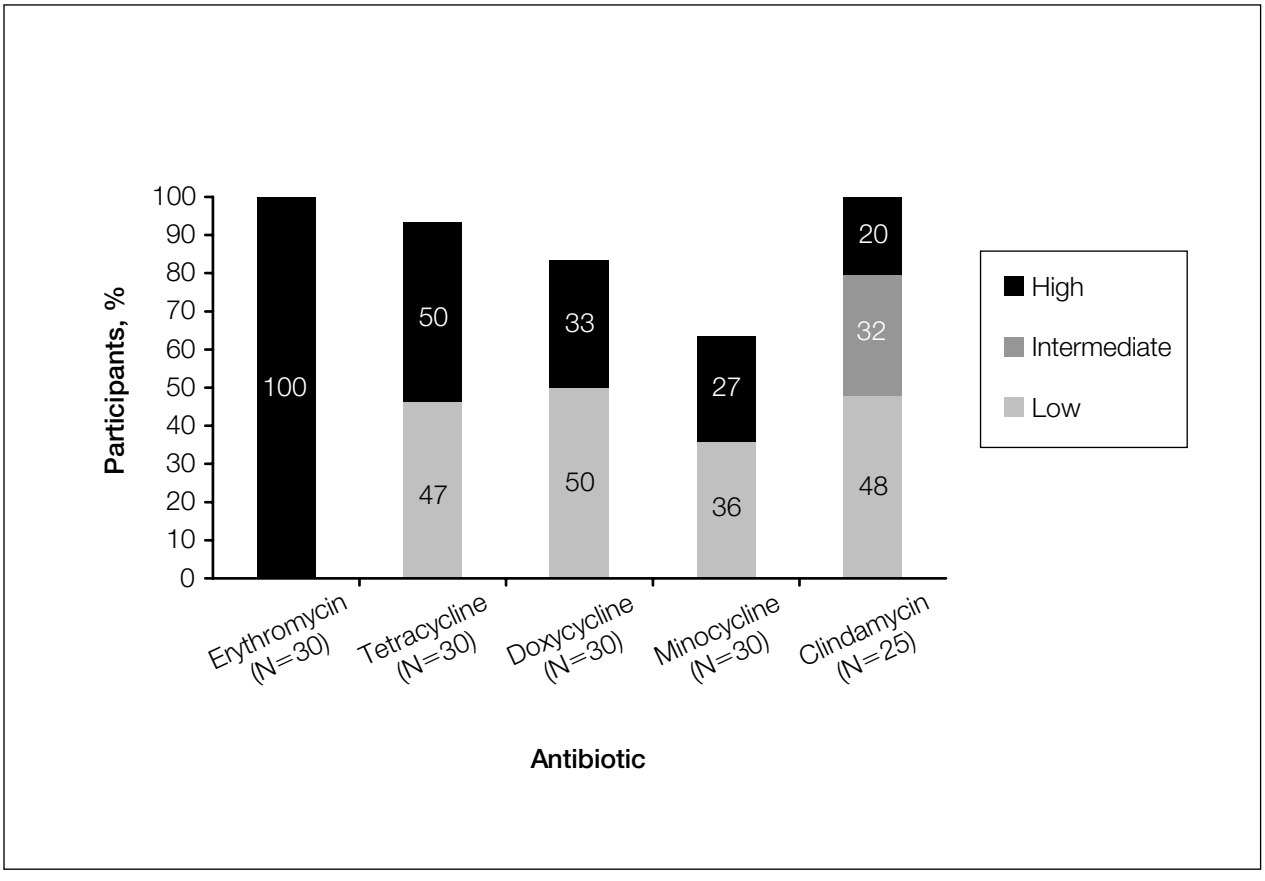


**Figure 1.** Participants with antibiotic-resistant *Propionibacterium acnes* strains identified at baseline. No individuals showed intermediate-level resistance to erythromycin and tetracyclines; a range of sensitivities was seen for clindamycin.

goal of therapy was to remove subsurface *P acnes*, a control group receiving the vehicle only was deemed unnecessary.

Quantitative cultures using a modified Williamson-Kligman scrub technique were obtained for 30 participants at baseline and after 1, 2, and 3 weeks of daily washing with BPO cleanser 6%.[17] Participants were required to have a *P acnes* population of 10,000 colonies/cm$^2$ or more as determined by culture at screening, with *P acnes* cultures resistant to erythromycin and tetracycline at 8 μg/mL or more and 2 μg/mL or more, respectively. Resistance was confirmed by culturing *P acnes* on *Brucella* agar plates containing erythromycin (8 μg/mL), tetracycline (2 μg/mL), doxycycline (2 μg/mL), or minocycline (2 μg/mL).[18] Minimum inhibitory concentration (MIC) levels for these antibiotics and clindamycin were determined by growth in agar plates with increasing concentrations of antibiotics. Culture samples from all 30 participants were tested at baseline for erythromycin, tetracycline, doxycycline, and minocycline resistance; samples from 25 participants were tested for clindamycin resistance. Participants were stratified based on low-, intermediate-, or high-level erythromycin, tetracycline family, or clindamycin resistance.

## Results

Samples from all 30 participants showed strains of *P acnes* with erythromycin MIC levels of more than 512 μg/mL (high). In the 25 samples tested for clindamycin resistance, 12 samples showed MIC levels ranging from 8 to 64 μg/mL (low), 8 samples showed MIC levels ranging from 128 to less than 512 μg/mL (intermediate), and 5 individuals had strains with MIC levels of 512 μg/mL or more (high). In the case of the tetracycline family, high-level resistance was most common for tetracycline but also was seen for doxycycline and minocycline (Figure 1).

Therapy with BPO cleanser 6% resulted in significant reductions in total *P acnes* counts and counts of erythromycin/clindamycin-, tetracycline-, doxycycline-, and minocycline-resistant strains after the first week of treatment ($P<.0001$, paired *t* test). Counts decreased by approximately 1 log after 1 week of treatment with the BPO cleanser 6%, by at least 1.5 log after 2 weeks of treatment,

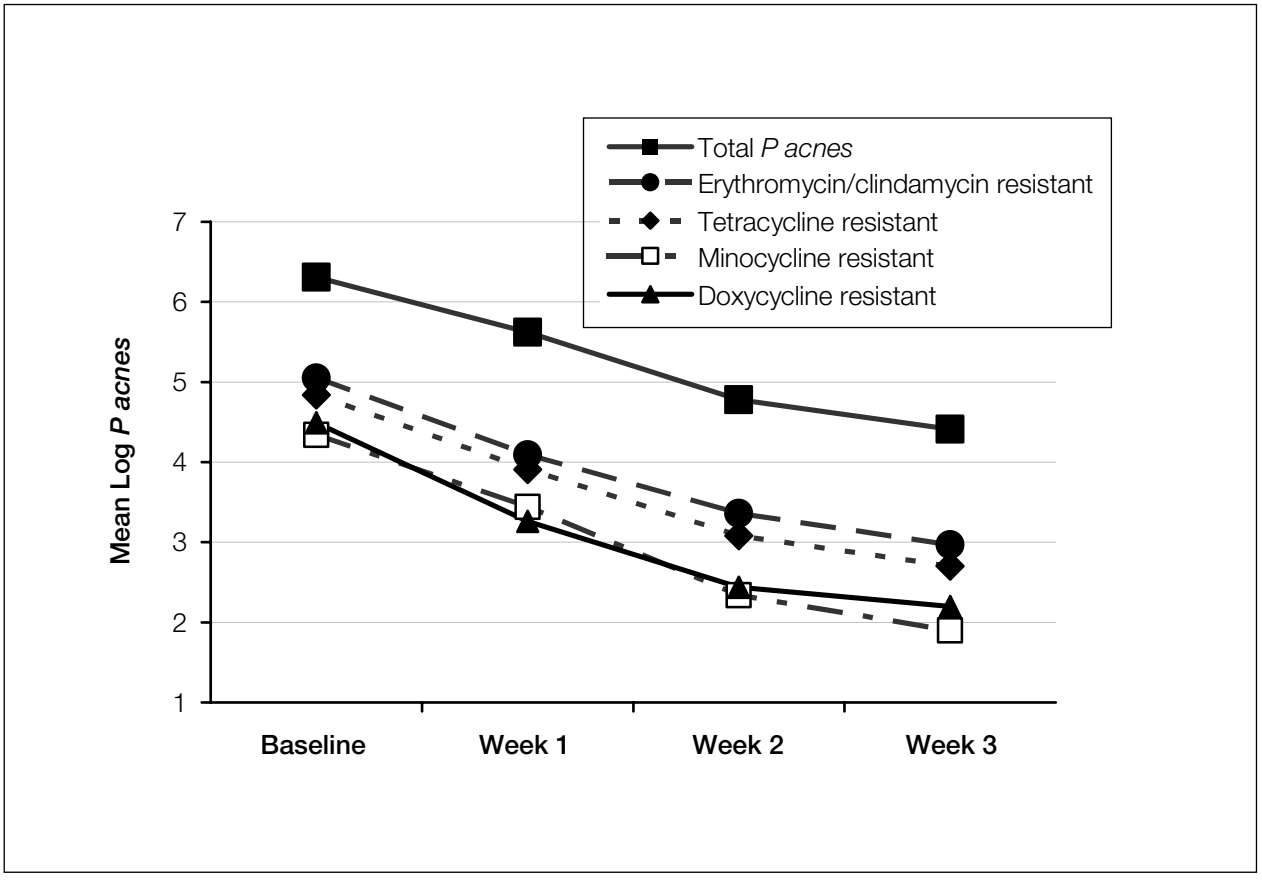


**Figure 2.** Effect of benzoyl peroxide cleanser 6% on total and antibiotic-resistant populations of *Propionibacterium acnes*. $P<.0001$ vs baseline for all time points and *P acnes* populations.

and by at least 2 log after 3 weeks of treatment (Figure 2). The effects of the BPO solution did not differ between low- and high-level resistant strains.

## Comment

These results demonstrate that once-daily 20-second applications of BPO cleanser 6% for 3 weeks are sufficient to produce a 2-log reduction in *P acnes* counts for both sensitive and resistant strains. The effectiveness of this formulation may result from several factors that promote retention of BPO on the skin after the wash has been rinsed off. First, although it is poorly soluble in water, BPO is highly lipophilic, a favorable characteristic for penetration into sebaceous follicles.[19] Second, the wash contains C12-15 alkyl benzoate, which is immiscible with water and may improve BPO retention.[20] The reduction in *P acnes* counts for BPO cleanser 6% is somewhat less than what has been reported for leave-on formulations (up to a 3-log reduction in *P acnes* populations).[13,21]

Although the short residence time may limit the effects of the BPO wash on *P acnes*, it also may enhance tolerability, ease of use, and adherence. Washes are relatively convenient compared with leave-on agents.[16] Contact with BPO may bleach clothing or hair,[22,23] effects that may be less likely with a wash than leave-on formulations. Use of a wash also can help avoid interactions with oxidation-sensitive medications such as some topical retinoids. Because the initial populations of resistant *P acnes* strains are usually relatively low, a 2-log reduction from a wash is likely to provide adequate control of the resistant populations, especially in view of the potential for better tolerability and adherence with a wash.

## Conclusion

Given the growing evidence of antibiotic resistance of *P acnes* on the skin of patients with acne, a BPO cleanser 6% provides clinicians and patients with a regimen that is effective against antibiotic-resistant *P acnes*. Combination therapy that includes a BPO cleanser 6% may be a useful therapeutic option for preventing or minimizing the development of antibiotic resistance and for controlling acne in patients with resistant *P acnes*.

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