What is the Role of Benzoyl Peroxide Cleansers in Acne Management?

Do they Decrease *Propionibacterium acnes* Counts? Do they Reduce Acne Lesions?

by James Q. Del Rosso, DO, FAOCD

Benzoyl peroxide (BPO) has been an important component of topical therapy for acne vulgaris for more than five decades due to its ability to markedly reduce *Propionibacterium acnes* and inflammatory acne lesions and its ability to moderately reduce noninflammatory acne lesions.[1–3] Unlike antibiotics, which induce alterations in bacterial structure, specific enzymes, and/or nuclear and cytoplasmic proteins, BPO is directly toxic to *P. acnes* and other bacteria.[2,3] As a result, BPO has not been associated with the development of *P. acnes* resistance.[1–5] In addition, studies with leave-on formulations of BPO demonstrate reduction in the emergence of antibiotic-resistant *P. acnes* strains in patients treated concurrently with topical antibiotics, such as erythromycin or clindamycin.[1–5]

BPO cleanser/wash formulations represented approximately 50 percent of prescriptions for BPO among dermatologists from 2003 through 2006.[5,6] Unlike a leave-on BPO formulation, such as a gel or cream, a BPO cleanser/wash is designed to be used during the process of washing the skin followed by rinsing. This raises the question of whether or not a BPO cleanser/wash is capable of inducing therapeutic benefit with limited skin contact time during washing and after rinsing.[6,7]

Can a benzoyl peroxide wash/cleanser reduce colony counts of *P. acnes*?

Data are limited on the microbiologic effects of available BPO cleanser/wash formulations.[6,7] Unfortunately, there are too few studies, and a lack of comparative studies among formulations, to definitively state that any BPO cleanser/wash that is randomly selected for treatment of acne vulgaris, including over-the-counter (OTC) products, can markedly reduce colony counts of *P. acnes*. A two-week *P. acnes* microbiologic study evaluating an older formulation of a specific BPO 5% wash (N=75) demonstrated a modest reduction (46%) of *P. acnes*.[7,8] Another two-week *P. acnes* microbiologic study of a different brand BPO 10% cleanser used twice daily (N=17) confirmed a 93.5-percent reduction of *P. acnes* at Day 5, and a 97.5-percent reduction of *P. acnes* at the end of the study (Day 15).[7,9] Importantly, in a skin-contact-time evaluation performed on a human skin model using the same BPO vehicle as the BPO 10% cleanser used in the microbiologic study discussed above, 20 seconds of skin contact time followed by up to three 10-second rinses with water resulted in epidermal deposition of BPO.[7]

Can a benzoyl peroxide wash/cleanser reduce antibiotic-resistant *P. acnes* strains?

The determination that BPO reduces the emergence of antibiotic-resistant *P. acnes* strains has been based primarily on studies evaluating combination *leave-on* topical gels containing BPO 5% and either erythromycin or clindamycin.[3–5] More recently, the ability of a BPO cleanser/wash formulation to reduce pre-existent antibiotic-resistant *P. acnes* was evaluated. A three-week, microbiologic, *in-vivo* study evaluated *P. acnes* reduction in 30 adult subjects who, at study entry, were determined to exhibit either high-level or low-level antibiotic

Table 1. Mean Log Reduction In *P. acnes*
Benzoyl Peroxide 6% Cleanser Once Daily x 3 Weeks[1,2]

P. acnes Strains	Baseline	Week 1	Week 2	Week 3
Total Counts (N=30)	6.31	5.62	4.78	4.41
Erythromycin-Resistant Strains (n=30)	5.05	4.09	3.36	2.97
Tetracycline-resistant strains (n=28)	4.84	3.91	3.06	2.70
Doxycycline-Resistant strains (n=25)	4.49	3.26	2.44	2.20
Minocycline-Resistant Strains (n=19)	4.34	3.44	2.34	1.90

[1]Data on File, Medicis Pharmaceutical Corporation, 2007. [2]Leyden JJ. The effect of benzoyl peroxide 6% wash on antibiotic-resistant Propionibacterium canes. Poster presentation. 31st Hawaii Dermatology Seminar. Wailea, Maui, Hawaii. March 3-9, 2007.

resistance to *P. acnes* tested with tetracycline, doxycycline, minocycline, and erythromycin, using recognized criteria based on minimum inhibitory concentrations (MICs).[10] All included subjects demonstrated a high degree of fluorescence of facial skin under Wood's lamp exposure at baseline demonstrating presence of high levels of *P. acnes* (colony counts >10,000/cm^2 on forehead skin). None of the subjects had received any topical or systemic antibiotics within four weeks of study entry or any retinoids within six months of study entry. At baseline, all 30 subjects exhibited high-level *P. acnes* resistance to erythromycin (MICs >512µg/mL). Among those with *P. acnes* strains resistant to tetracycline (n=28), 15 and 13 subjects were shown to exhibit high-level resistance (MICs >8µg/mL) and low-level resistance, respectively. Twenty-five subjects were found to have strains of *P. acnes* resistant to doxycycline, with 10 demonstrating high-level resistance (MICs >8µg/mL) and 15 showing low-level resistance. Minocycline-resistant *P. acnes* strains were found in 19 subjects, with eight and 11 demonstrating high-level resistance (MICs >8µg/mL) and low-level resistance, respectively.

All subjects in the study utilized the specified brand BPO 6% cleanser once daily for facial cleansing, which was supervised by designated and trained personnel Monday through Friday at the study center.[10] On Saturday and Sunday, subjects completed facial cleansing once daily at home on their own. Treatment was administered in a standardized manner. At each use of the BPO 6% cleanser, the subjects wet their faces and liberally applied the cleanser while working up a full lather with particular attention given to the forehead region. They gently massaged the cleanser into the skin for 10 to 20 seconds, then rinsed their faces with water and patted dry. Using the modified Kligman-Williamson technique, quantitative *P. acnes* cultures were obtained at baseline, and at Weeks 1, 2, and 3 from a test site on the forehead. Determination of *P. acnes* organism counts were obtained at each time point.

The results from this *P. acnes* microbiologic study, as depicted in Table 1, demonstrated *in vivo* that the brand BPO 6% cleanser markedly reduced the colony counts of *P. acnes* strains shown prior to treatment to be resistant to one or more antibiotics that are commonly prescribed to treat acne vulgaris.[10] At baseline, 29 of 30 subjects demonstrated *P. acnes* resistance to more than one antibiotic. A steady reduction in total *P. acnes* counts, inclusive of both antibiotic-sensitive and antibiotic-resistant strains, was noted over the three-week duration of BPO 6% cleanser use. There was nearly a 2-log reduction after three weeks of treatment. Erythromycin-resistant *P. acnes* strains, found to be highly resistant in all 30 subjects, steadily declined over the course of the study, with a mean net reduction of 2 log noted after three weeks of therapy. Tetracycline-insensitive strains of *P. acnes* exhibited a steady reduction throughout the study with a mean net reduction of 1.8 log after two weeks, and 2 log after three weeks of treatment. Doxycycline- and minocycline-insensitive *P. acnes* strains both decreased steadily over the three-week course of treatment, with mean net log reductions at three weeks of 2.36 and 2.4, respectively.

Has use of a benzoyl peroxide cleanser/wash been shown to be effective in the treatment of acne vulgaris?

Data from studies evaluating the efficacy of BPO cleanser/wash formulations are limited, including products available by prescription or OTC.[6,7] In 56 subjects with facial acne vulgaris, a brand BPO 6% cleanser used once daily in the morning and tretinoin 0.1% microsphere gel applied once daily at night (n=30) was compared to the same retinoid applied once daily at night without use of the BPO 6% cleanser (n=26).[11] The 12-week study was investigator blinded. In both study arms, subjects were administered a designated nonmedicated gentle facial cleanser to be used, except in the morning in subjects randomized to the BPO cleanser study arm, and all subjects received a designated noncomedogenic SPF15 sunscreen. At Week 12, the mean percent reduction in inflammatory acne lesions was 58.5 percent in the group using both the BPO 6% cleanser and the topical retinoid, as compared to a 29.8-percent reduction in the topical retinoid monotherapy study group. This approximately twofold difference between both study groups was statistically significant (p=0.003). In the study arm using both the BPO 6% cleanser and tretinoin microsphere gel 0.1%, the investigators noted a favorable reduction in perilesional erythema. Signs of facial skin irritation, such as erythema, peeling, and dryness, were not increased overall in the study group using the BPO 6% cleanser and the topical retinoid as compared to monotherapy with the topical retinoid.

In subjects with truncal acne vulgaris (N=40) involving the back, chest, and/or shoulders, reduction in acne lesions were evaluated with monotherapy use of either a brand BPO 8% wash or a brand BPO 9% cleanser.[12] The study was investigator blinded and completed over a four-week period. The severity of truncal acne vulgaris was rated as moderate severity. In the group using the BPO 8% wash, the mean percent reductions in inflammatory and noninflammatory acne lesions at end of study (4 weeks) were 37.23 percent and 28.03 percent, respectively. In the group using the BPO 9% cleanser, the mean percent reductions in inflammatory and noninflammatory acne lesions at end of study (4 weeks) were 30.19 percent and 25.23 percent, respectively. Skin tolerability was favorable with both formulations.

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