Benzoyl Peroxide Cleansers for the Treatment of Acne Vulgaris: Status Report on Available Data

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Benzoyl peroxide (BPO) cleansers are commonly prescribed for treatment of acne vulgaris. In fact, they represent approximately half of all BPO prescriptions from dermatology practices. Data are limited on the ability of BPO cleansers to reduce counts of Propionibacterium acnes, *impact on reduction and emergence of antibiotic-resistant* P acnes *strains, and efficacy for facial and truncal acne vulgaris. This article discusses available data on BPO cleanser formulations.*

Cutis. 2008;82:336-342.

Benzoyl peroxide (BPO), available for clinical use for more than 50 years, continues to be extensively utilized worldwide as a topical agent for the treatment of acne.[1,2] The extensive use of BPO relates to its ability to substantially reduce counts of the bacterium *Propionibacterium acnes*; reduce counts of inflammatory and noninflammatory acne lesions; potentiate the effect of antibiotic therapy; reduce emergence of *P acnes* strains that are less sensitive to commonly prescribed antibiotics such as tetracyclines, erythromycin, and clindamycin; and prevent proliferation of preexistent antibiotic-resistant *P acnes* strains.[1-5] To date, *P acnes* organisms resistant to BPO have not been identified,[1,2] which is related to the direct toxic effect induced by BPO rather than an antibiotic mechanism that may be associated with selection pressure or pathways of resistance that are "learned" and transferred by bacteria after prolonged antibiotic exposure.

The ability of BPO gels to reduce acne lesion counts and suppress *P acnes* is well-established.[1,2] However, the ability of specific BPO cleansers to produce true clinical benefit by suppressing *P acnes*, reducing acne lesion counts, and providing additional benefit when used in combination with other topical agents as a component of the therapeutic program has not been fully appreciated.[6] Importantly, BPO cleansers and washes comprised approximately 50% of the total number of BPO formulations prescribed by dermatologists based on data from 2003-2006 (Figure 1).[7] Although proprietary formulations of BPO cleansers and washes specifically use the terms *cleanser* or *wash* as a formal part of their trade names, these designations refer to therapeutic BPO formulations that are used during the process of cleansing or washing the skin followed by rinsing, as opposed to leave-on formulations (eg, gel, cream, lotion) that are applied to and left on the skin. For the purpose of this article, the term *cleanser* will be used to encompass both BPO cleanser and wash formulations.

What are the implications of brand versus nonbrand BPO cleansers?

Overall, data on clinical efficacy and microbiologic effects, such as *P acnes* organism count reduction,

Accepted for publication August 12, 2008.

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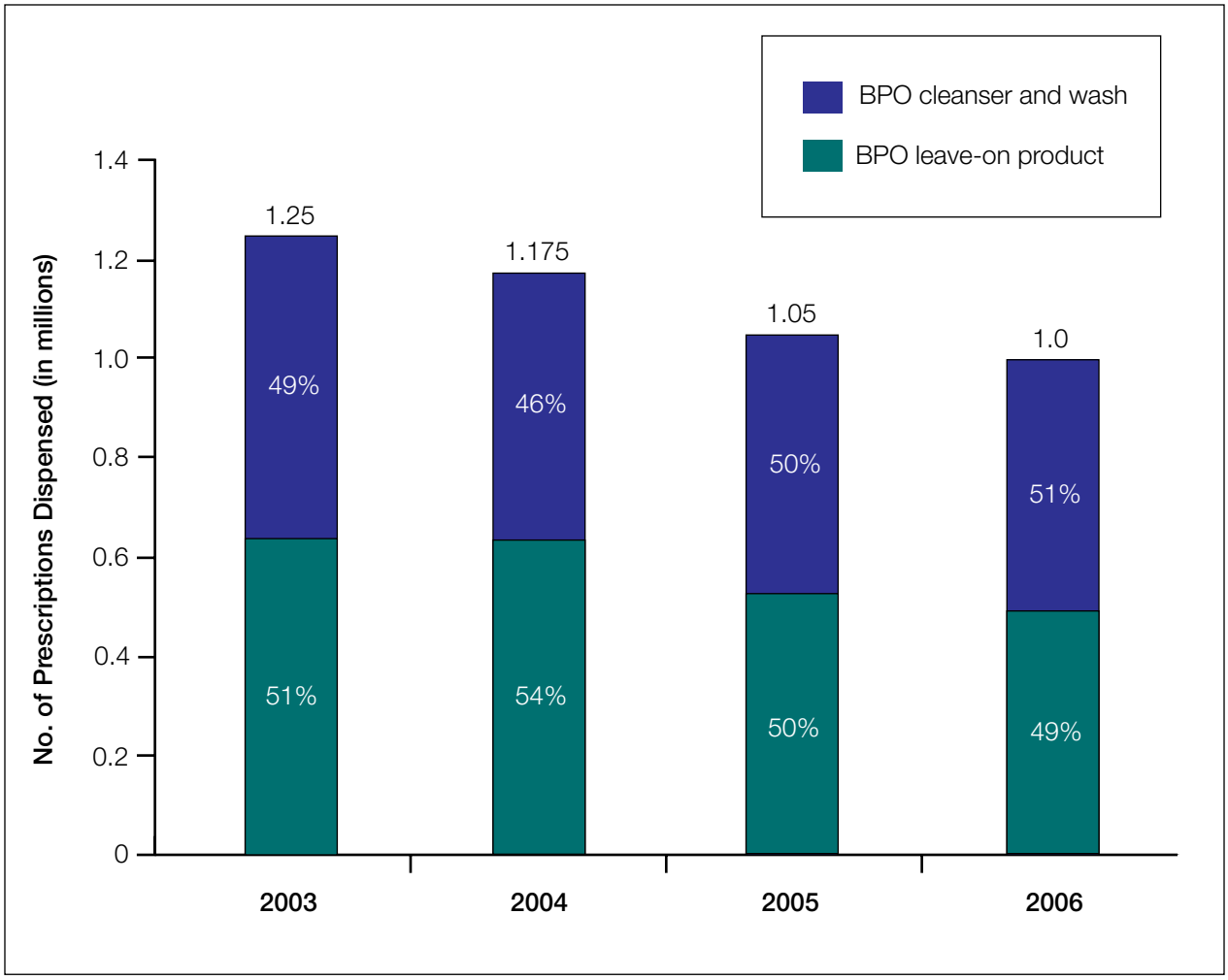

Figure 1. Total number of prescriptions dispensed by dermatologists (2003-2006) for benzoyl peroxide (BPO) cleansers and washes as well as leave-on products.

are limited with BPO cleansers.[6] The data available in individual studies present results achieved with specific brand formulations. As vehicle characteristics may markedly influence the cutaneous deposition, delivery, and pharmacokinetic properties of active ingredient with topical formulations, it is not scientifically appropriate to assume that results achieved in a study performed using one specific brand formulation of a BPO cleanser are applicable to other brand or nonbrand cleansers.[2,6,8]

What data are available on *P acnes* organism count reduction with BPO cleansers?

In a study evaluating the use of BPO wash 5% (Benzac®) monotherapy in participants with acne vulgaris, *P acnes* reduction was determined (N=75). Microbiologic assays demonstrated a 46% reduction in *P acnes* organism counts after 2 weeks, which is considered to be a modest decrease.[6,9]

Benzoyl peroxide cleanser 10% (Triaz®) was evaluated in participants treated for acne vulgaris twice daily for 2 weeks to quantify the reduction in *P acnes* organism counts using an established methodology (N=17).[10] Substantial reductions in *P acnes* counts were observed as early as day 5, with continued *P acnes* suppression demonstrated at completion of the study. At day 5, *P acnes* was reduced from a log count of 6.39 (2,450,000 organism count) to a log count of 5.18 (156,000 organism count), correlating with a 93.5% reduction in *P acnes*. At day 15, a further decrease to a log count of 4.84 was observed (68,835 organism count), indicating a 97.1% reduction in *P acnes*.[10] Although of a lesser magnitude than the leave-on gel counterparts, these levels of *P acnes* reduction achieved with the BPO cleanser 10% formulation approach those levels achieved with BPO gel 6% and BPO gel 10% formulations and exceed *P acnes* reduction values reported with

Baseline Antibiotic Resistance Characteristics of Tested *Propionibacterium acnes* Strains[23]

Antibiotic	Participants, n	High-Level Resistance, n	Low-Level Resistance, n
Tetracycline	29	15	14
Doxycycline	25	10	15
Minocycline	19	8	11
Erythromycin	30	30	–

the use of clindamycin phosphate lotion 1% and azelaic acid cream 20%.[10-12]

What are the potential implications of the emergence of *P acnes* strains that are less sensitive to antibiotics used to treat acne vulgaris?

It is well-documented that over time the prevalence of *P acnes* strains that are less sensitive to commonly prescribed antibiotics for the treatment of acne vulgaris such as tetracyclines, erythromycin, and clindamycin has increased.[1,2,13-19] The clinical significance of these antibiotic-resistant strains is the observation that their emergence in some cases may correlate with decreased efficacy of therapy in some patients.[2,15,18] On the other hand, the consistency of the correlation of *P acnes* antibiotic resistance with decreased therapeutic effectiveness among the overall acne treatment population continues to be a matter of debate as some antibiotics in use for 3 or more decades, such as clindamycin, minocycline, and doxycycline, continue to demonstrate efficacy over time.[2,20,21]

Nevertheless, preventing the emergence of antibiotic-resistant bacteria during acne treatment remains an important practical consideration.[1,5,21,22] Concomitant topical application of BPO with erythromycin or clindamycin has been shown to augment the decrease in *P acnes* colony counts and reduce the emergence of antibiotic-resistant strains of *P acnes* using leave-on combination gel formulations.[1,2,13,22] In one study, a specific formulation of BPO cleanser 6% (Triaz) markedly reduced counts of *P acnes* strains shown at baseline to be resistant to tetracycline, doxycycline, minocycline, and/or erythromycin.[23] The ability of BPO to decrease *P acnes* organism counts, including antibiotic-resistant strains, has led to the recommendation to use BPO in combination with antibiotic therapy when the latter is prescribed for acne vulgaris, especially with prolonged therapy.[1,2,15,22]

Can a BPO cleanser substantially reduce the number of antibiotic-resistant *P acnes* organisms?

This question was addressed in a 3-week study evaluating *P acnes* reduction in participants who exhibited either high-level or low-level *P acnes* antibiotic resistance to tetracycline, doxycycline, minocycline, and/or erythromycin at baseline and were treated once daily with BPO cleanser 6% (N=30).[23] The distribution of antibiotic-resistant *P acnes* strains at baseline is depicted in the Table. All participants were instructed to wash their face once daily with BPO cleanser 6%. Facial cleansing by all study participants was supervised and observed at the study site by designated and trained personnel Monday through Friday and participants cleansed at home on Saturday and Sunday unsupervised. Quantitative cultures were obtained using the modified Williamson-Kligman technique at baseline and weeks 1, 2, and 3, allowing for determination of *P acnes* organism counts at each time point. The results demonstrated in vivo the ability of the specific BPO cleanser 6% to markedly reduce the colony counts of *P acnes* strains that were resistant at baseline to one or more antibiotics commonly prescribed to treat acne vulgaris (Figure 2).[23]

Has clinical efficacy been demonstrated with use of a BPO cleanser for the treatment of acne vulgaris?

In a double-blind vehicle-controlled study assessing the effect of monotherapy with BPO wash 5% on inflammatory acne lesion counts, participants used the wash twice daily for a 12-week period (N=75). In the group treated with the BPO wash 5%, a 39% reduction in inflammatory lesion counts was

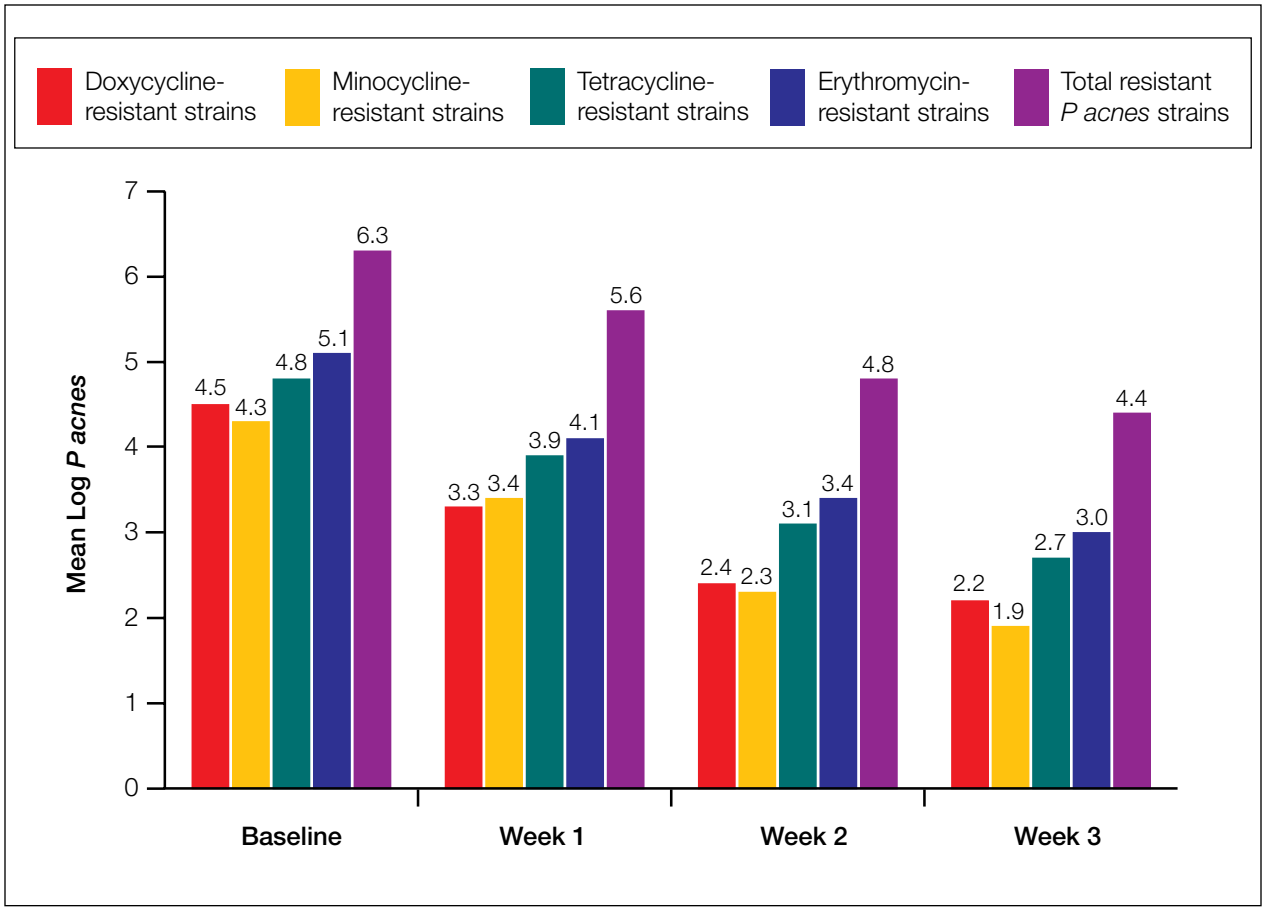

Figure 2. Effect of benzoyl peroxide cleanser 6% on antibiotic-resistant *Propionibacterium acnes* counts. Participants were treated once daily with the cleanser for 3 weeks. Log *P acnes* reduction values are rounded to the nearest tenth.[23]

observed compared to a less than 10% reduction in the vehicle group.[9]

A 12-week randomized, controlled, investigator-blind, parallel group clinical trial examined the potential therapeutic benefit and tolerability of a designated BPO cleanser when used in combination with a topical retinoid (tretinoin microsphere gel 0.1%) in participants with facial acne vulgaris (N=56).[24] The combination of BPO cleanser 6% used in the morning and tretinoin microsphere gel 0.1% in the evening (n=30) was compared to application of tretinoin microsphere gel 0.1% alone in the evening (n=26). Both groups were given a designated gentle nonlipid, nonmedicated facial cleanser to be used in the morning and evening, except for those participants randomized to use the BPO cleanser 6% in the morning. All study participants were instructed to apply a designated noncomedogenic, broad-spectrum sunscreen in the morning approximately 5 minutes after washing, with additional applications allowed as needed. Analyzed study parameters included acne lesion counts; erythema associated with acne lesions (perilesional erythema); and features of treatment-associated cutaneous irritation such as erythema, peeling, and dryness. At the 12-week study end point, participants using both BPO cleanser 6% and tretinoin microsphere gel 0.1% demonstrated a percentage reduction in inflammatory lesion counts that was approximately 2-fold greater than participants treated with the topical retinoid alone (Figure 3), with these results shown to be statistically significant ($P<.01$). Improvement in perilesional erythema also was noted and a favorable tolerability profile was observed similarly in both study groups. In this study, the use of the BPO cleanser 6% in combination with tretinoin microsphere gel 0.1% did not result in an overall increase in skin irritation compared to monotherapy with tretinoin microsphere gel 0.1%.[24]

In a study of 696 participants, approximately half (52.3%) of participants with facial acne vulgaris also exhibited truncal involvement, primarily mild to moderate in severity.[25] A 4-week investigator-blinded clinical trial reported the mean percentage change in noninflammatory and inflammatory lesion

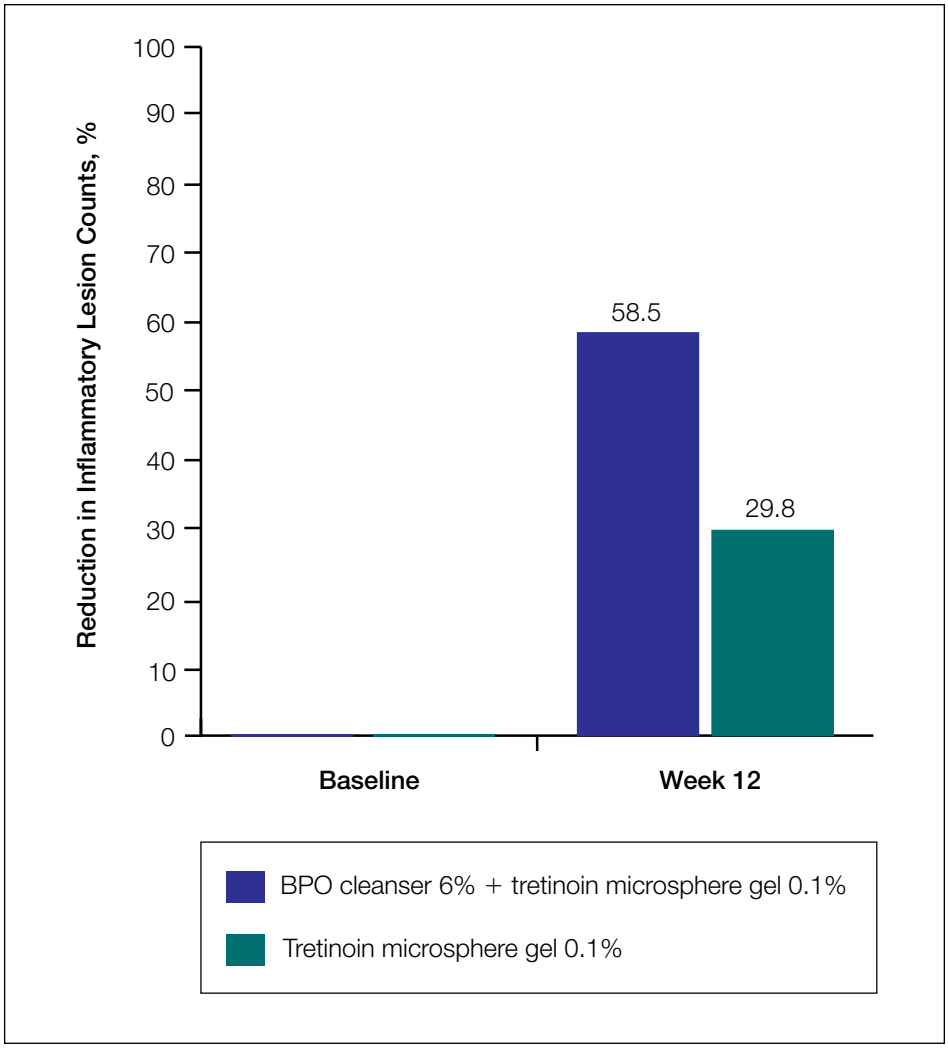

Figure 3. Reduction in inflammatory acne lesion counts with benzoyl peroxide (BPO) cleanser 6% in the morning and tretinoin microsphere gel 0.1% in the evening versus tretinoin microsphere gel 0.1% monotherapy in the evening. The combination treatment group experienced a statistically significant greater reduction in inflammatory lesion counts compared to the monotherapy group ($P<.01$).[24]

count reductions in participants (N=40) with truncal acne vulgaris treated with either the creamy wash formulation of BPO 8% (Brevoxyl®) or BPO cleanser 9% (Triaz).[26] All participants presented with truncal acne rated as moderate in severity, with involvement of the back, chest, and/or shoulders. Efficacy results are presented in Figure 4. Both cleanser formulations were well-tolerated.[26] This study, despite its short duration of treatment, provides data supporting clinical efficacy with these BPO cleanser formulations for truncal acne vulgaris. This information is clinically relevant because the use of a therapeutically active cleanser is highly adaptable and convenient for treatment of acne vulgaris involving the trunk because of the need to treat a more extensive body surface area.

Are data available on BPO cleanser use and skin contact time?

Although a BPO cleanser may be proven to be effective in a controlled study scenario, success in clinical practice requires understanding and education regarding proper use. Typically, patients are instructed to gently massage the cleanser onto lightly moistened skin and allow for reasonable contact time, followed by gentle rinsing.[6] The definition of "reasonable" contact time is not consistently defined for all products and well-designed studies correlating specific contact times with clinical efficacy are lacking overall for BPO cleansers.

An in vitro human skin study of a designated BPO cleanser 6% (Triaz) demonstrated that a contact time of 20 seconds allowed for cutaneous deposition and penetration of BPO.[27] The study utilized excised human cadaver skin in a Franz-type diffusion cell and radiolabeled BPO formulated in a 6% cleanser. After a 20-second application of the cleanser with water, deposition and penetration of BPO was demonstrated on the surface and within the stratum corneum after a variety of application methods, including after 1 and 2 successive 10-second rinse cycles and after 1, 2, and

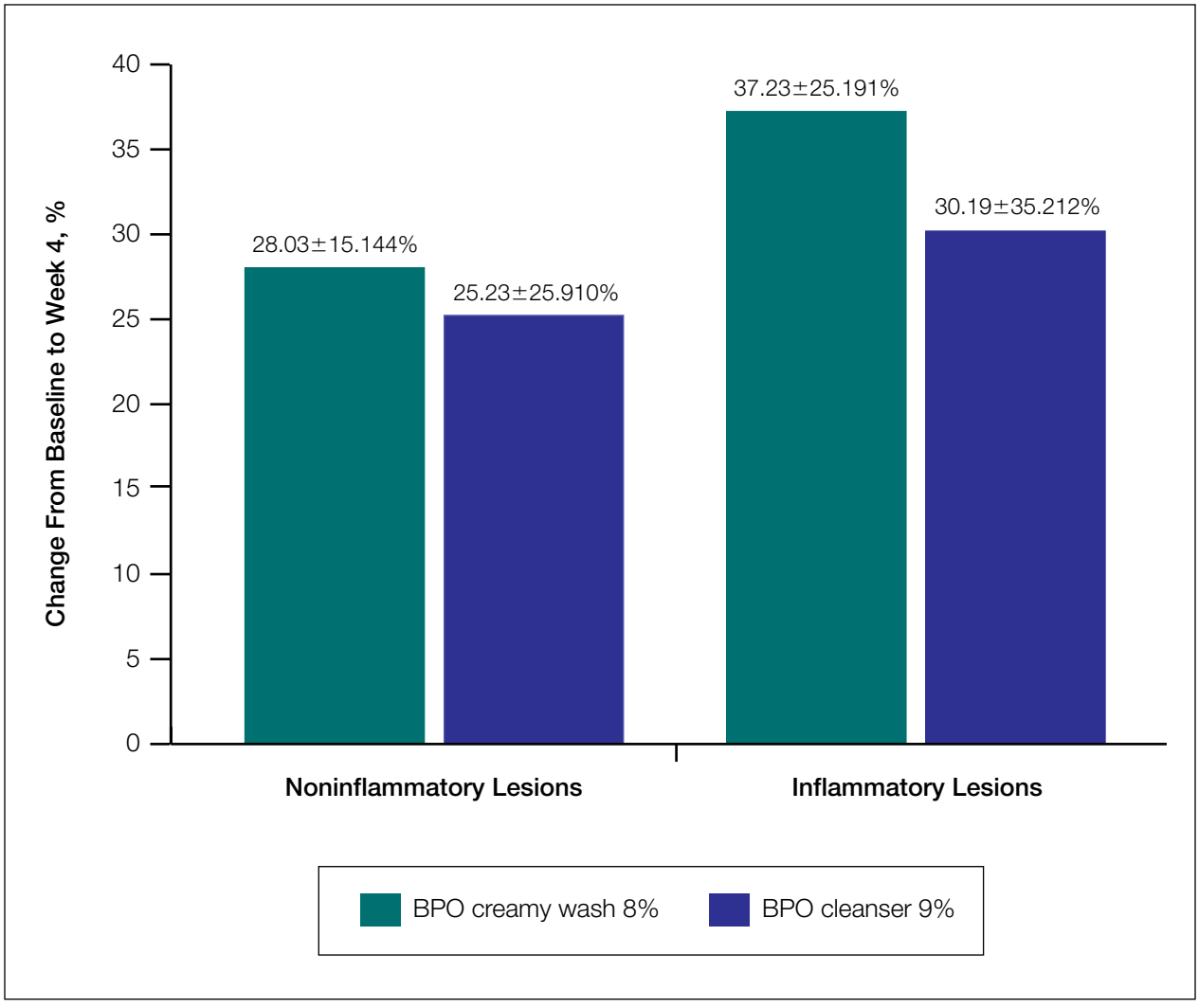

Figure 4. Reduction of noninflammatory and inflammatory acne lesions with benzoyl peroxide (BPO) creamy wash 8% versus BPO cleanser 9% for the treatment of truncal acne vulgaris.[26]

3 successive cycles that combined skin rubbing followed by 10-second rinsing. These application methods were designed to simulate patient usage of the cleanser.[27] When explaining the proper use of this BPO cleanser formulation to a patient, the "20-10 approach" of gentle massage application to lightly moistened skin (a 20-second contact time) and gentle rinsing over an approximate 10-second period is both rational and time efficient.[6] This approach also avoids vigorous and prolonged rubbing, both of which can induce unwanted irritation.

Conclusion

Available data support the consideration of using a BPO cleanser as an option when selecting a topical combination therapy regimen. Because most patients being treated for acne vulgaris are instructed to cleanse, use of an effective and well-tolerated BPO cleanser may reduce the number of treatment steps, enhance compliance, and allow for BPO usage in patients experiencing too much irritation with leave-on BPO formulations applied to the face. Additionally, use of a BPO cleanser for treatment of truncal acne vulgaris is efficient because of the need to treat a more extensive body surface area. This latter point may be of greater clinical importance in patients on oral antibiotic therapy for acne vulgaris with both facial and truncal involvement.

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