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A randomized, single-blind comparison of topical clindamycin + benzoyl peroxide and adapalene in the treatment of mild to moderate facial acne vulgaris

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Conflicts of interest

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Summary

Background Antibiotics are often combined with other agents to provide topical acne treatments that are effective against both inflammatory and noninflammatory lesions and minimize the development of antibiotic resistance. Retinoids and associated treatments also have anti-inflammatory activity and decrease microcomedo formation. To date, few direct comparisons of these different acne treatments have been conducted.

Objectives To compare the clinical effectiveness of two treatments for facial acne: a ready-mixed once-daily gel containing clindamycin phosphate 10 mg mL^{-1} + benzoyl peroxide 50 mg mL^{-1} (CDP + BPO; Duac®; Stiefel, High Wycombe, U.K.) and a once-daily gel containing adapalene 0·1% (ADA; Differin®; Galderma, Watford, U.K.).

Methods In this assessor-blind, randomized study; 65 patients were treated with CDP + BPO once daily and 65 patients with ADA once daily. The treatment period was 12 weeks and lesion counts, acne grade and global improvement were assessed at weeks 1, 2, 4, 8 and 12.

Results CDP + BPO showed an earlier onset of action with a faster significant reduction in inflammatory and total lesion counts than ADA. A between-group comparison of the percentage change from baseline showed that CDP + BPO was statistically significantly superior to ADA from week 1 onwards both for inflammatory lesions ($P \leq 0{\cdot}001$) and for total lesions ($P \leq 0{\cdot}004$). While 76% of inflammatory lesions remained at week 2 for patients using ADA, in contrast, only 55% of inflammatory lesions remained at week 2 in the CDP + BPO group, resulting in a treatment effect of 1·38. Thus CDP + BPO removed 38% more inflammatory lesions than ADA at this timepoint. The trend in favour of CDP + BPO, although less marked, continued to the end of the study. CDP + BPO was better tolerated than ADA, with a greater proportion of ADA-treated patients experiencing treatment-related adverse events. Adjunctive topical or oral agents and their impact on acne were not studied in this trial. Due to product differences, this study could not be double blinded but was only single (assessor) blinded.

Conclusions CDP + BPO and ADA are both effective treatments for acne, but CDP + BPO has a significantly earlier onset of action, is significantly more effective against inflamed and total lesions and is better tolerated, which should improve patient compliance.

Both topical and systemic antimicrobial therapy have been a mainstay of acne treatment for many years, with topical antibiotics being indicated for patients with mild to moderate inflammatory acne. Clindamycin and erythromycin are the two most widely used antibiotics.[1]

The current consensus is that topical antibiotics alone should not be used as monotherapy in acne because of their relatively slow onset of action and their potential for causing bacterial resistance.[2] Widespread use of topical formulations of erythromycin and clindamycin has resulted in a significant distribution of cross-resistant strains of propionibacteria in Europe.[3] Furthermore, topical antibiotic therapy can induce or select resistance in coagulase-negative staphylococci: Harkaway *et al.*[4] found that after 12 weeks of treatment with topical erythromycin, the cutaneous aerobic flora was dominated by *Staphylococcus epidermidis* which was completely resistant to erythromycin and showed increased resistance to clindamycin and tetracycline.

As acne is characterized by both inflammatory and noninflammatory lesions, strategies have been developed to combine an antibiotic with a treatment which is effective against noninflammatory lesions and which will minimize the risk of the development of resistance. Benzoyl peroxide is one such treatment: it is mildly keratolytic and is effective against noninflammatory lesions. It is an antimicrobial agent that effectively suppresses *Propionibacterium acnes* and alone significantly improves inflammatory acne. There is no evidence that microorganisms become resistant to benzoyl peroxide and it is equally effective against antibiotic-resistant and antibiotic-sensitive bacteria.[5] The combination of benzoyl peroxide with erythromycin or clindamycin has been shown to be clinically more effective and better tolerated than benzoyl peroxide or antibiotic alone.[6–9] Not only are these combinations more effective in reducing counts of *P. acnes*, but they also do not select antibiotic-resistant variants.[7,8,10] Furthermore, treatment with benzoyl peroxide and a combination of erythromycin and benzoyl peroxide resulted in a significant reduction in cutaneous staphylococci without any change in resistance pattern to erythromycin and other antibiotics.[4]

Adapalene is a synthetic naphthoic acid derivative with retinoid activity, which has been shown to reverse the abnormal follicular desquamation and inflammatory responses involved in the pathogenesis of acne.[11–15] The efficacy of adapalene has been established in several clinical trials. In particular, studies have been conducted to compare adapalene with its first-generation topical retinoid compound, tretinoin 0·025% gel, in the treatment of acne vulgaris. In a meta-analysis of five multicentre studies involving a total of 900 patients, it was demonstrated that after 12 weeks of treatment, both agents were equally effective in reducing the total number of acne lesions.[16] Furthermore, adapalene demonstrated more rapid efficacy and was associated with significantly less skin irritation than tretinoin.

There is a plethora of medications used to treat acne; however, therapeutic challenges remain and, as such, it is important that research into effective treatment strategies for this disease continues. In this study, we compared the efficacy and safety of two topical products as monotherapy: a ready-mixed once-daily gel containing clindamycin phosphate 10 mg mL^{-1} + benzoyl peroxide 50 mg mL^{-1} (CDP + BPO; Duac®; also known as Clindoxyl and Indoxyl; Stiefel, High Wycombe, U.K.) and a once-daily gel containing adapalene 0·1% (ADA; Differin®; Galderma, Watford, U.K.).

Materials and methods

Study design

This was a multicentre, randomized, single-blind, parallel-group comparison of CDP + BPO and ADA. The study was conducted at one centre in Poland (Zespol Naukowa Badawczy, Iwonicz Zdroj) and one centre in the U.K. (Leeds General Infirmary) with a further centre in the U.K. providing consultancy advice (Hammersmith Hospital, London).

Patients were assessed at admission (week 0) and at weeks 1, 2, 4, 8 and 12 (or sooner, in the event of early withdrawal).

The study and all appropriate amendments were reviewed and approved by the appropriate regulatory and ethics committees in Poland and the U.K. and the study was performed in accordance with the Declaration of Helsinki (South Africa, 1996 amendment) and Good Clinical Practice guideline. Subjects aged 16 years or older provided written informed consent to participate; subjects under 16 years gave assent and their parents/guardians provided consent.

Patients

Male and female patients aged 12–39 years with mild to moderate acne vulgaris of the face, with at least 15 inflammatory and/or noninflammatory lesions but no more than three nodulocystic lesions and an acne grade[17] of ≥2·0 and <7·0, were eligible. Patients agreed not to use sun beds or to undergo ultraviolet (UV) treatment, to minimize exposure to direct sunlight and to limit alcohol consumption to 14 units $week^{-1}$ for the duration of the study. Patients who were using antiandrogen-containing contraceptives, who had received oral or topical steroids, oral or topical antibiotics, or acne treatment of any kind, in the previous month, including natural or artificial UV therapy, or did so at any stage of their participation in the trial, were excluded, as were those who had participated in any clinical trial within 30 days of recruitment into the study. Other exclusion criteria included those that could interfere with the evaluation of study treatment (such as disease of facial skin) and those that would safeguard the subject (history of regional enteritis or ulcerative colitis or history of antibiotic-associated colitis). Only one member of a household was allowed to participate.

The planned number of patients was based upon the expected percentage difference in reduction/improvement in inflammatory lesion counts at week 2. It was expected that the percentage reduction/improvement in inflammatory lesion counts

at week 2 would be 42·0% for CDP + BPO and 22·8% for ADA (i.e. a percentage difference of 19·2%). Statistical testing for superiority was anticipated (with 80% power and a 5% significance level) assuming corrected calculations with Fisher's exact test. In total, 65 patients per group were required on this basis.

Study treatments

Patients were assigned to treatment groups in a 1 : 1 ratio using a predetermined computer-generated randomization schedule with a block size of six. Within each country, patients were randomized to each treatment in equal numbers. Patients in both groups applied the medication once daily in the evening. The facial skin had first to be thoroughly washed, rinsed with warm water and gently patted dry. Treatment was then applied over the entire affected area. The scheduled treatment period was 12 weeks. To maintain blinding, a separate study nurse or pharmacist was responsible for dispensing study medication and for instructing the patient on the proper method of application.

Assessments

Treatment efficacy was determined by noninflammatory and inflammatory lesion counts; lesion counts were made of the whole face. Macules were not included in lesion counts and noninflammatory lesions were not counted on the chin or nose. In certain situations, lesion counts were conducted for a specific area of the face only; in such cases the same area was used throughout the study. Lesion counts were made for restricted areas in the event that facial hair caused problems. If numerous (>100) noninflammatory lesions were present, part of the face could be chosen for an individual patient for the noninflammatory lesion count but inflammatory lesions were counted for the whole face. Assessors were trained in this procedure which was rigorously enforced throughout the study.

The physician evaluated acne grade according to the Leeds Revised Acne Grading System.[17] At each visit, the physician assessed global change from baseline as: very much improved, much improved, minimally improved, no change, minimally worse, much worse or very much worse. Patients rated their condition as: improved, no change or worse. In the U.K., the skin surface bacteria of the face were sampled at admission and final assessment visit using the detergent scrub wash method of Williamson and Kligman.[18] The same area of the cheek or forehead was sampled on each occasion; sampled bacterial flora were tested for viable P. *acnes*, clindamycin-resistant P. *acnes* and erythromycin-resistant P. *acnes* on anaerobically incubated plates.

Adverse events were recorded throughout the study and their severity and relationship to treatment were assessed. In addition, information on certain signs and symptoms was solicited. Physicians rated scaling, erythema and dryness and patients rated pruritus and burning as none, mild, moderate or severe and, if present, as intermittent or persistent. Any tolerance parameter classified as 'severe' was recorded as an adverse event. Overall tolerance was assessed as poor, fair, good or excellent at the end of the study. Adverse events were coded using MedDRA (version 8.01) (MedDRA, IFPMA, MS80, Reston, VA, USA).

All assessors were blinded to the treatment received. Prestudy training was used to standardize assessments. To optimize consistency of subjective evaluations, the same staff saw the same patients at each of their visits, whenever possible.

Statistical analysis

All data analysis was carried out according to a pre-established analysis plan. As an early onset of action is critical for the success of acne therapies, the primary efficacy variable was the absolute values and the percentage change from baseline in inflammatory lesion counts at week 2. Secondary endpoints were the absolute values and percentage change from baseline in inflammatory lesion counts at weeks 1, 4, 8 and 12 and in noninflammatory and total lesion counts at all postbaseline assessments. The absolute and percentage change from baseline was assessed using the Mann–Whitney test. Supportive analysis of the primary endpoint was undertaken using a general linear model. The categorical efficacy measures—global change, patient's self-rating and acne grade—were compared between groups using two-sided Cochran–Mantel–Haenszel χ^2 tests.

Missing data were imputed using last observation carried forward. All comparisons of treatment groups used two-tailed hypothesis tests at the 5% level of significance. No adjustments were made for multiplicity. Patient data below are presented for the intent-to-treat (ITT) population only.

Results

Patient disposition and baseline characteristics

In total, 130 patients (65 patients in each group) were randomized to treatment and assessed between December 2004 and August 2005, inclusive. One hundred and twenty patients (92·3%) completed the study, with the main reasons for discontinuation being noncompliance and unavailability for follow-up (see Fig. 1). The two treatment groups were well matched with respect to demography (Table 1).

The mean ± SD duration of acne vulgaris was 6·06 ± 4·153 years for patients in the CDP + BPO group and 5·45 ± 3·653 years for patients in the ADA group. As the acne had a somewhat longer mean duration for those in the CDP + BPO group it thus might be regarded as more intransigent in that group.

Most patients (80%) had been treated previously for acne vulgaris. The most common prior treatment was adapalene, which had been administered to 32·3% of the CDP + BPO group and 23·1% of the ADA group (Table 1).

Lesion counts and efficacy evaluations

For both treatment groups, a progressive decline was observed in the number of inflammatory and noninflammatory lesions.

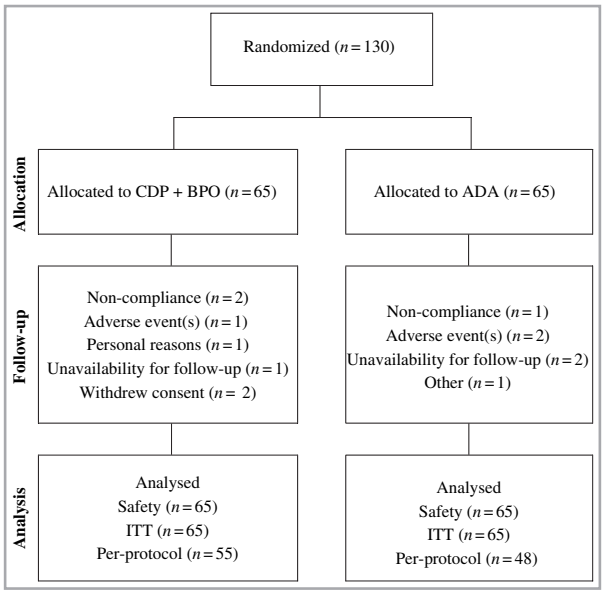

Fig 1. Flow diagram. CDP, clindamycin phosphate; BPO, benzoyl peroxide; ADA, adapalene; ITT, intent-to-treat.

The improvements (absolute values and median percentage reduction) in lesion counts are shown in Table 2 and Figure 2, respectively. The difference between groups for the percentage change from baseline was statistically significantly different at week 1 onwards for inflammatory lesions ($P \leq 0{\cdot}001$), in favour of CDP + BPO, and was also statistically significantly different at week 1 onwards for total lesions ($P \leq 0{\cdot}004$), again in favour of CDP + BPO.

The expected proportion of inflammatory lesions left at week 2 (determined using a general linear model) is 0·76 for ADA (after adjusting for baseline and centre). This means that 76% of inflammatory lesions were left at week 2 for patients using ADA. In contrast, the study demonstrated that, for CDP + BPO, only 55% of inflammatory lesions remained at week 2, resulting in a treatment effect of 1·38. This implies that CDP + BPO removed 38% more inflammatory lesions than ADA at this timepoint. The 95% confidence interval is 1·15–1·66, which lies wholly higher than 1·0, and the P-value is 0·001. Both statistics imply that CDP + BPO is significantly superior to ADA for the ITT population at week 2. The percentage reduction in inflammatory lesion counts is shown in Figure 2b.

Acne grade decreased in both treatment groups; however, this decrease was more significant with CDP + BPO, with statistical significance ($P = 0{\cdot}013$) being achieved as early as week 1 and being maintained throughout the course of the study ($P \leq 0{\cdot}038$; Table 3).

In the assessment of global change, the majority of patients showed at least minimal improvement from week 1 onwards. The proportion classified as very much or much improved increased over the study period in both groups; however, early during treatment (weeks 1 and 2), the percentage who were very much or much improved was greater with CDP + BPO treatment (Fig. 3). A statistically significant difference in favour of CDP + BPO was found from week 1 onwards ($P \leq 0{\cdot}007$).

Table 1 Baseline characteristics (intent-to-treat population)

	CDP + BPO (n = 65)	ADA (n = 65)
Sex		
Males	27 (41·5%)	27 (41·5%)
Females	38 (58·5%)	38 (58·5%)
Age (years)		
Mean ± SD	21·4 ± 4·50	21·8 ± 4·75
Range	13–33	13–38
Race		
Caucasian	63 (96·9%)	65 (100·0%)
Asian	2 (3·1%)	0 (0·0%)
Inflammatory lesion counts		
Mean ± SD	34·3 ± 18·13	35·3 ± 19·82
Median (range)	30 (15–107)	28 (15–106)
Noninflammatory lesion counts		
Mean ± SD	60·9 ± 41·11	58·6 ± 37·83
Median (range)	51 (9–169)	50 (13–176)
Total lesion counts		
Mean ± SD	95·2 ± 48·76	93·9 ± 48·20
Median (range)	89 (30–223)	87 (34–282)
Acne grade		
Mean ± SD	3·442 ± 0·8475	3·404 ± 0·8668
Median (range)	3 (2–6)	3 (2–6)
Most common previous treatments (>10%)		
Adapalene	21 (32·3%)	15 (23·1%)
Lymecycline	17 (26·2%)	12 (18·5%)
Benzoyl peroxide	13 (20·0%)	14 (21·5%)
Zineryt®	9 (13·8%)	9 (13·8%)
Dianette®	4 (6·2%)	13 (20·0%)
Erythromycin	8 (12·3%)	9 (13·8%)
Tetracycline	8 (12·3%)	8 (12·3%)
Isotretinoin	8 (12·3%)	6 (9·2%)
Clindamycin phosphate	4 (6·2%)	8 (12·3%)

CDP, clindamycin phosphate; BPO, benzoyl peroxide; ADA, adapalene.

The patient's assessment of improvement showed a similar pattern of change to the physician's rating. The percentage that rated themselves as improved increased over time to about 90% by the end of the study for both treatment groups. As in the physician's rating, the proportion improved was greater early in treatment (weeks 1, 2, 4 and 8) with CDP + BPO ($P < 0{\cdot}05$).

The limited amount of bacteriology data from the U.K. showed a progressive decline in propionibacteria with CDP + BPO which was not demonstrated with ADA (Table 4). The development of resistance appeared to decline with CDP + BPO treatment, but to increase with ADA.

Tolerance and safety evaluations

In general, both treatment regimens were well tolerated with a few notable differences. CDP + BPO generally gave

Table 2 Absolute lesion counts (intent-to-treat population)

	CDP + BPO		ADA	
	Mean ± SD	n	Mean ± SD	n
Total number of noninflammatory lesions				
Week 0	60·9 ± 41·11	65	58·6 ± 37·83	65
Week 1	57·1 ± 42·69	64	57·3 ± 39·70	65
Week 2	48·2 ± 36·69	65	52·0 ± 40·37	64
Week 4	42·6 ± 36·48	63	44·0 ± 34·38	64
Week 8	35·0 ± 33·22	61	38·6 ± 31·36	62
Week 12	31·6 ± 38·43	60	30·0 ± 24·33	61
Total number of inflammatory lesions				
Week 0	34·3 ± 18·13	65	35·3 ± 19·82	65
Week 1	26·3 ± 19·24	64	31·4 ± 19·58	65
Week 2	22·0 ± 15·74	65	28·7 ± 20·63	64
Week 4	16·8 ± 13·96	63	27·1 ± 19·99	64
Week 8	16·6 ± 19·37	61	22·9 ± 21·49	62
Week 12	12·5 (19·15)	60	17·8 ± 18·66	61
Total number of lesions				
Week 0	95·2 ± 48·76	65	93·9 ± 48·20	65
Week 1	83·4 ± 54·69	64	88·7 ± 50·60	65
Week 2	70·2 ± 45·52	65	80·7 ± 53·09	64
Week 4	59·4 ± 45·96	63	71·1 ± 47·10	64
Week 8	51·6 ± 47·30	61	61·5 ± 46·78	62
Week 12	44·1 ± 50·10	60	47·8 ± 39·25	61

CDP, clindamycin phosphate; BPO, benzoyl peroxide; ADA, adapalene.

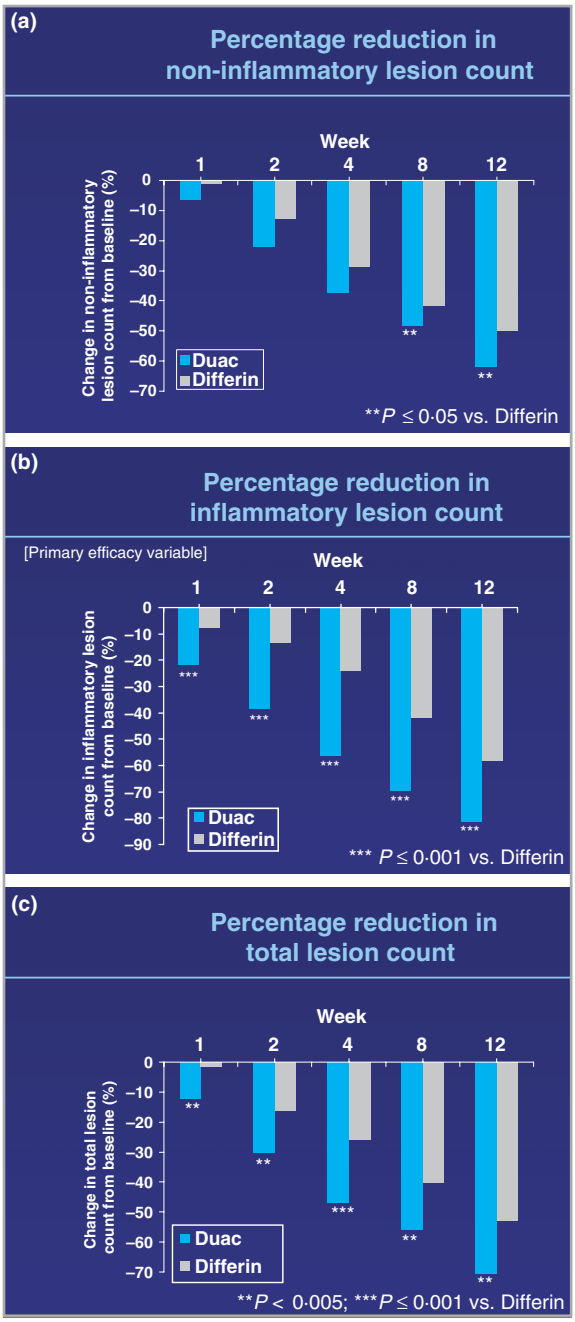

Fig 2. The median improvements in lesion counts from baseline for (a) noninflammatory lesions, (b) inflammatory lesions and (c) total lesions (intent-to-treat population: n = 65). Differences between groups tested using the Mann–Whitney test.

fewer occurrences of scaling, erythema, dryness and burning. Occurrences of pruritus were evenly distributed between groups. Most signs/symptoms in each group were mild and persistent/continuous.

For the majority of patients, overall tolerance at week 12 for both treatments was rated as good or excellent. The overall assessment of tolerance by the investigator showed that 77·0% of patients in the CDP + BPO group were rated as having good or excellent tolerance. However, in the ADA group only 52·3% of patients were in these categories.

The number of patients who reported at least one treatment-emergent adverse event was distributed evenly between the treatment groups: 21 patients (32·3%) in the CDP + BPO group and 20 patients (30·8%) in the ADA group. In total, 16 patients (12·3%) experienced adverse events considered by the investigator to be possibly related to study medication. More patients in the ADA group (10 patients; 15·4%) experienced these than patients in the CDP + BPO group (six patients; 9·2%).

In the CDP + BPO group, the investigator recorded a definite relationship with treatment in one (1·5%) patient. This was a general disorders and administration site condition (application site burning, erythema and dryness). In the ADA group, seven (10·8%) patients had an adverse event which was considered to be definitely related to treatment: general disorders and administration conditions (application site burning, dryness, erythema, desquamation, dermatitis, pain, pruritus and reaction) and skin and subcutaneous tissue disorders (skin burning sensation).

Two patients, one patient in each group, experienced adverse events leading to withdrawal from the study. One patient in Poland (treated with CDP + BPO) experienced application site erythema, burning and pruritus which was considered definitely related to the study medication. One patient in the U.K. (treated with ADA) experienced application

Table 3 Acne grade (mean ± SD; intent-to-treat population)

	CDP + BPO (n = 65)	ADA (n = 65)
Week 0	3·44 ± 0·85	3·40 ± 0·87
Week 1	2·68 ± 1·12	3·18 ± 1·08
Week 2	2·38 ± 1·14	2·86 ± 1·24
Week 4	2·00 ± 1·07	2·86 ± 1·28
Week 8	1·59 ± 0·96	2·36 ± 1·49
Week 12	1·09 ± 0·84	1·99 ± 1·70

CDP, clindamycin phosphate; BPO, benzoyl peroxide; ADA, adapalene.

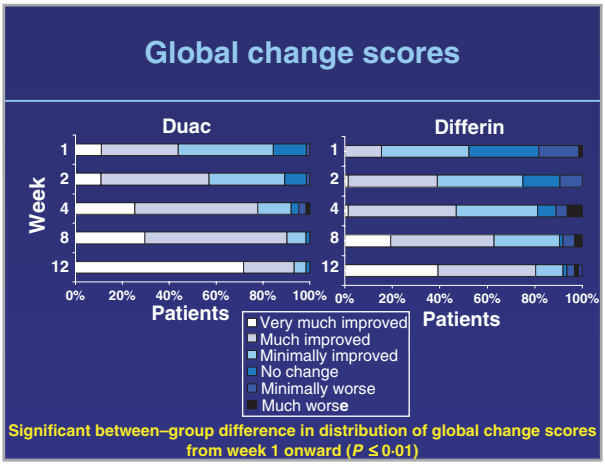

Fig 3. Global change score (intent-to-treat population: n = 65). Differences between groups tested using Cochran–Mantel–Haenszel tests.

Table 4 Bacteriology (intent-to-treat population)

	Total number of propionibacteria (log_{10} CFU cm^{-2})	
	CDP + BPO (n = 20)	ADA (n = 20)
Admission	4·370	4·412
Week 12/discontinuation	3·130	4·914
Resistance: number of resistant propionibacteria (log_{10} CFU cm^{-2})		
Erythromycin		
Admission	1·999	2·162
Week 12/discontinuation	1·093	2·288
Clindamycin		
Admission	1·634	1·441
Week 12/discontinuation	0·832	1·528

CFU, colony-forming units; CDP, clindamycin phosphate; BPO, benzoyl peroxide; ADA, adapalene. Resistance is presented as the number (%) of subjects with any nonzero value recorded for resistant bacteria. The number of resistant bacteria is presented as the mean.

site dermatitis which was considered definitely related to the study medication.

Discussion

The results from this study demonstrate an improvement in both the inflammatory and noninflammatory lesions of acne over a 12-week treatment period with the two topical therapies used. A difference between therapies was apparent in the first week of treatment, with once-daily CDP + BPO being associated with greater improvement in inflammatory lesion counts, total lesion counts and acne grade than ADA. These statistically significant differences between treatments were maintained over the 12 weeks in favour of CDP + BPO.

The earlier onset of action of the CDP + BPO combination may well promote patient compliance, particularly as it is a ready-mixed gel requiring only once-daily application. Compliance, efficacy and simplicity of dosage regimen are closely related. Efficacy depends upon good dosing compliance and good compliance follows from convenience in use and treatment tolerability. Failure to follow use instructions is thought to be a major reason for acne treatment failure,[19] and medication adherence is critical to efficacy.[20] During maintenance therapy, simplicity of the regimen and tolerability of the treatment become more important.[20] Some investigators note the importance of patient preference in choosing an acne formulation;[21] other studies have suggested that once-daily treatment and first time use encourage compliance.[22] However, compliance was not directly studied nor verifiable with the data gathered from this study.

Both treatments were well tolerated. Benzoyl peroxide is generally regarded as irritant; however, the combination of CDP + BPO was better tolerated than ADA. The good tolerability of CDP + BPO may be related to the formulation of the gel which includes a moisturizer and to the direct anti-inflammatory action of clindamycin, which could alleviate the irritancy of benzoyl peroxide.[23]

The greater efficacy of CDP + BPO over ADA may be associated with the greater ability of benzoyl peroxide to penetrate acne lesions, thus exposing bacteria to higher concentrations of both bacteriostatic agents.[24,25] In the case of the CDP + BPO formulation, the reduction in inflammation, associated with the reduction in bacteria and the suppression of bacterial release of free fatty acids and other chemotactic factors, may well be assisted by the suppression of leucocyte chemotaxis shown to occur *in vitro* with clindamycin.[26] In support of these hypotheses, the data from our study suggest that benzoyl peroxide inhibits the rise in resistant bacteria that can occur with topical antibacterial treatment, and further recent evidence shows that the combination of CDP + BPO has a greater anti-propionibacterial effect than erythromycin + zinc (unpublished data). Further investigations would be required to confirm any differences between CDP + BPO and ADA in this regard. We also speculate that the mild keratolytic effect of benzoyl peroxide has a significant effect on cell differentiation,

resulting in a more rapid onset of healing of both inflammatory and noninflammatory lesions.

The results of this study show some important differences between therapy with CDP + BPO and ADA from both an efficacy and a safety perspective that have significance for physicians and patients. Of greatest importance to patients with acne is rapid onset of action of a medication, and of greatest importance to physicians is the assurance that a medication will work safely and reliably. This study demonstrated that CDP + BPO has a greater potential to satisfy both of these groups than does ADA. More specifically, CDP + BPO therapy resulted in a statistically significantly greater reduction in lesions by week 1 than ADA therapy, and this difference in favour of CDP + BPO persisted over the treatment period. This was achieved in the face of a better safety profile for the CDP + BPO treated group. The CDP + BPO group was noted by the patients and the investigators to tolerate the treatment better than the ADA group. These results have great importance for the choice of therapy for both the patient with acne and the prescribing physician. Adolescents often abandon acne treatments prematurely because of a slow onset of action, irritation or inconvenience in use. The favourable safety profile, rapid onset of action and once-daily dosing regimen of CDP + BPO will improve compliance and, therefore, efficacy.

Recent guidelines have promoted the use of topical retinoids as first-line and maintenance therapy for the treatment of acne, with topical antimicrobials being used in combination with topical retinoids for mild papular/pustular acne only.[2] These same guidelines recommend the use of oral antibiotics in combination for moderate acne. With there being a greater concern regarding the use of systemic antibiotics and the development of resistance, CDP + BPO is indicated for the topical treatment of both mild and moderate acne vulgaris and should be considered, with[27] or without topical retinoids, as first-line therapy for the treatment of the majority of cases of acne vulgaris. Although ADA inhibits the formation of and reduces the number of microcomedones, the greater anti-inflammatory activity of both CDP and BPO promotes an earlier response to treatment.

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