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Antibiotic Sensitivity of *Cutibacterium acnes* Isolates from Acne Patients in a Skin Hospital in Singapore

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Abstract

Background: The increasing use of antibiotics for acne has led to the development antibiotic resistant propionobacteria and has become a worldwide problem in the recent years.

Objective: We investigated the prevalence and pattern of antibiotic resistance to *Cutibacterium acnes (C. acnes)* and its relation to previous antibiotic therapy in acne patients attending the dermatology outpatient clinic in a tertiary dermatological referral Centre in Singapore.

Methods: Skin swabs were collected from the skin lesions in 402 acne patients at baseline, 2months and 4 months. Cultures for *C. acnes* were done and sensitivity testing of the isolates was done using 5 commonly used antibiotics, namely tetracycline, minocycline, doxycycline, erythromycin and clindamycin. Data was collected about the previous treatment and current treatment being prescribed from Centre during these visits.

Results: *Cutibacterium acnes* were isolated in 241 (60%) acne patients at baseline. Sixty seven (28.5%) of 235 isolates were resistant to at least one antibiotic. Clindamycin resistance was most common (n=64, 27.2%), followed by erythromycin (n=63, 26.8%), doxycycline (n=22, 9.4%), tetracycline (n=14, 6.0%) and minocycline (n=4, 1.7%). Previous use of antibiotics was significantly more in patients with resistant strains of *C. acne* (59.7%) as compared to those who had sensitive strains (44.0%) (P=0.03). Individually, the use of oral erythromycin and minocycline was significantly more in patients who harbored resistant strains (23.9% *vs.* 8.9%; P<0.01: 9.0% *vs.* 2.4%; P=0.04 respectively). There was no significant difference in the acne severity between the patients who had resistant *P. acne* strains versus those who had sensitive strains.

Conclusion: Antibiotic resistant *C. acnes* are prevalent in Singapore. Clindamycin and erythromycin resistance were most commonly seen among the resistant strains. Past history of antibiotic use especially erythromycin and minocycline was commonly seen among the patients who harbored resistant strains.

Keywords: *Propionobacterium acnes*; Acne; Antibiotic sensitivity

Introduction

Acne is one of the most common skin problems affecting more than 85% of adolescents and often also continues into adulthood. *Cutibacterium acnes* (*C. acnes*) is a gram positive, non-spore forming anaerobic bacilli with predominant inhabitation of the sebaceous region and plays an important role in the pathogenesis of acne vulgaris [1,2] Antibiotics inhibits the growth of *P. acnes* and/or the production of inflammatory mediators and have been used as the mainstay for inflammatory acne vulgaris since many years [3,4]. The earliest evidence for antibiotic resistant *P. acnes* started emerging from the late 1970s and thereafter has been reported in various parts of the world [4-8]. The chronicity of the disease, antimicrobial administration route, the duration of therapy, poor treatment compliance, and easy access to therapeutic agents without medical supervision are some of the factors that have contributed to the development of antibiotic resistance [8-11]. Antibiotic-resistant *C. acnes* may also spread from patients to close contacts [9]. It has also been shown to associate with a poor treatment outcome [10]. Also, antibiotic-resistant genes when passed from *C. acnes* to other skin inhabitors like *Staphylococcus aureus* and *Streptococcus pyogenes*, may have public health implications [11]. Treatment of acne patients with topical and systemic antibiotics is a common practice in Singapore. Previous studies were done in Singapore to determine the epidemiology of acne among adolescents, *C. acnes* isolation rate and *C. acnes* resistance patterns [12,13]. Data from these studies reflected that the resistance to antibiotics seemed to reflect antibiotic prescription trends. The mean MIC of the isolates tended to be higher in patients with history of prior antibiotic therapy. Other study done at the same Centre depicted that antibiotic resistance can occur with short term antibiotic courses and the rate of resistance increases as the duration of antibiotic consumption increases [14].

The aim of this study was to estimate the local prevalence of *C. acnes* amongst acne patients, and evaluate levels of antimicrobial resistance to the most frequently prescribed antibiotics. The study also aimed to determine if antibiotic resistance correlates clinically with treatment failure or therapeutic response. Attempt was also made to analyze the extent and progression of antimicrobial resistance over time.

Materials and Methods

Subjects

Patients with acne vulgaris, 12 years or more of age with clinical evidence of comedonal or inflammatory acne on the face and/or the trunk attending National Skin Centre (tertiary dermatological referral Centre) in Singapore were invited to participate in the study. Written consent was obtained from the patients after detailed explanation. Basic clinical information, including age, gender, age of onset and previous treatment history, was obtained at the time of patients' entry into the study or subsequently retrieved from the consultation records. The study was approved by the institutional review board. The reference ID provided to the study by the National healthcare group Domain specific Review board was 2007/00422.

The study consisted of 3 visits, each visit spaced 2 months apart. At each visit, acne severity was graded as mild (<20 comedones, or <15 inflammatory lesions, or total lesion count <30) moderate (20-100 comedones, or 15-50 inflammatory lesions, or total lesion count 30-125) and severe (>5 cysts, or total comedo count >100, or total inflammatory count >50, or total lesion count >125) according to lesional count as proposed by Lehmann et al. [15] Data was collected about the previous treatment and current treatment being prescribed from the Centre. At each visit, sampling was carried out from the patient's face and/back for isolation of *C. acnes*. If *C. acnes* were detected on culture, antibiotic sensitivity testing was performed on these isolates using 5 antibiotics, namely tetracycline, minocycline, doxycycline, erythromycin, and clindamycin. Topical or systemic antibacterial agents were prescribed if the dermatologist deemed clinically necessary. Treatment was not influenced by any of the microbiological results obtained from isolation of *C. acnes* from the subjects' skin.

Specimen collection, culture and antibiotic sensitivity testing

The surface of the entire face and/or affected areas on the back was rubbed with a transport swab moistened in 0.075 mol/L sodium phosphate buffer containing 0.1% Triton-X 100. Samples were inoculated on Schaedler agar and incubated anaerobically at 35°C for 5 days in anaerobic jars (GasPak anaerobic system, BBL, USA). Suspicious colonies were sub-cultured onto TSA sheep blood agar. Colonies found to be pleomorphic, catalase positive, and spot indole positive were identified with the RapID ANA II system (Oxoid, UK).

MICs of doxycycline, minocycline, tetracycline, clindamycin and erythromycin were determined with the E test method on Brucella base agar with 5% laked sheep blood, 5 mg/L hemin and 1 mg/L VitK1 (Oxoid, UK). Plates were incubated anaerobically at 35°C, and read at 48 hrs. Susceptibility breakpoints followed were those recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and Clinical and Laboratory Standards Institute [16,17].

Statistical Analysis

Prevalence of positive cultures for *C. acnes* in from patients with acne and their antibiotic sensitivity to tetracycline, doxycycline, minocycline, erythromycin and clindamycin were summarized using descriptive statistics, together with acne severity, previous acne medications and antibiotics used. Chi-square tests were used to compare the clinical characteristics and treatments between patients with positive *P. acnes* and those with negative smears. Fisher's exact test was used if the expected value in any of the cells of a contingency table was below [5]. Clinical characteristics, treatments and antibiotic resistance of *C. acnes* in patients with positive cultures were analyzed across the visits and tested using generalized estimating equations. p-value<0.05 was considered statistical significant. Statistics was generated using Stata version [14].

Results

A total of 402 patients of acne were recruited into the study, comprising of 113 males, 61 females and 228 children. Of these, 393 patients completed the study, 7 withdrew from the study at visit 2 and 2 patients at visit [3].

Prevalence, acne severity and treatment history

Cutibacterium acnes (*C. acnes*) were isolated in 60% of all acne patients at baseline. This accounted for 241 of the 402 patients. At the baseline, 87 patients (21.6%) had mild acne, 26 (6.5%) had mild to moderate acne, 250 (62.2%) had moderate acne, 6 (1.5%) had moderate to severe acne and 33 (8.2%) had severe acne respectively.

A history of previous use of acne creams was present in 225 (56%), and history of previous antibiotic use was present in 204 (50.7%) of the patients. 138 patients used 1 antibiotic, 53 patients used 2, 12 patients used 3 and 1 patient used 4 antibiotics. The mean number of antibiotics used at baseline was 0.7+0.8. The most commonly used acne cream was topical tretinoin (29.3%) followed by topical benzoyl peroxide (23.4%), sulphur & resorcinol cream/lotion (15.2%), adapalene (10.7%), topical clindamycin (13.7%), topical erythromycin (3.0%), topical BP+clindamycin combination (2.5%) and topical adapalene+benzoyl peroxide combination (0.8%). Among the oral medications, the most commonly used was doxycycline (29.4%), followed by erythromycin (12.9%), oral isotretinoin (7.9%), minocycline (4.7%), tetracycline (1.7%), trimethoprim +sulphomethoxazole (1.2%) and cephalexin, amoxicillin and augmentin (0.3%) each.

There was no significant difference in the acne severity, previous acne cream and antibiotics used between patients who harboured *C. acnes* on culture as compared to those who were negative for *C. acnes* at baseline, except for the use of topical clindamycin antibiotic was significantly higher in culture negative patients (18.1% *vs.* 10.8%; P=0.04).

Results of antibiotic susceptibility testing

At baseline, 67 (28.5%) of 235 patients with positive cultures were found to be resistant to at least one antibiotic (Table 1). The highest proportion of patients were resistant to clindamycin (n=64, 27.2%), followed by erythromycin (n=63, 26.8%), doxycycline (n=22, 9.4%), tetracycline (n=14, 6.0%) and minocycline (n=4, 1.7%). The mean MIC at baseline was highest to erythromycin (65.54+111.78) followed by clindamycin (45.44+97.07). Also, among the cyclines, highest mean MIC was for doxycycline (1.85+17.07), followed by tetracycline (0.76+3.92), and minocycline (0.14+0.46). There was no significant difference in the acne severity between the patients who cultured resistant *P. acne* strains as compared to those who had sensitive strains.

Antibiotics	No. of subjects	% of all isolates	% of resistant isolates	Mean MIC (mg/L)
Clindamycin	64	27.2	95.5	45.44

Erythromycin	63	26.8	94.2	65.54
Doxycycline	22	9.4	32.8	1.85
Tetracycline	14	6	20.8	0.76
Minocycline	4	1.7	5.9	0.14
Resistant breakpoints: Clindamycin 0.25 mg/L; Erythromycin 0.5 mg/L; Tetracycline 2 mg/L; Doxycycline and minocycline 1 mg/L.				

Table 1: Antibiotic resistance pattern of *Propionobacterium acnes* isolates at baseline.

Antibiotic susceptibility pattern in relation to previous antibiotic therapy for acne

Overall, the previous use of antibiotics was significantly more in patients who harbored resistant strains of *P. acne* (59.7%) as compared to those who had sensitive strains (44.0%) (P=0.03). Looking at each antibiotics individually, the difference in the antibiotic use was statistically significant only for oral erythromycin (23.9% *vs.* 8.9%; P<0.01) and minocycline (9.0% *vs.* 2.4%; P=0.04), both of them being used more frequently by the patients harboring resistant strains (Table 2).

Previous h/o antibiotic use for acne	Resistant isolates n=67	Sensitive isolates n=168	p-value
Any antibiotic	40 (59.7%)	74 (44%)	0.03
Clindamycin (topical)	11 (16.4%)	15 (8.9%)	0.1
Erythromycin (Oral)	16 (23.9%)	15 (8.9%)	<0.01
Erythromycin (Topical)	3 (4.5%)	5 (3.0%)	0.69
Doxycycline	17 (25.4%)	46 (27.4%)	0.75
Tetracycline	1 (1.5%)	3 (1.8%)	1
Minocycline	6 (9%)	4 (2.4%)	0.02
All values are expressed as number and percentage (%).			

Table 2: Comparision of previous antibiotic therapy among resistant and sensitive isolates of *P. acnes* at baseline.

Extent, progression and pattern of antimicrobial resistance over time and relation to current antibiotic treatment

Patients with a positive culture for *C. acnes* at baseline were followed up at 2 months (visit 2) and 4 months (visit 3) and analysis was done with respect to the severity of acne, use of acne medications and antibiotic susceptibility. Of the 241 patients for whom *C. acnes* was isolated at visit 1, data for resistance analysis was available for 235 patients at visit 1, 74 patients at visit 2, and 52 patients at visit 3.

There was an overall increase in the usage of topical acne creams (68.1% *vs.* 54.4%; P<0.01) and oral antibiotics (68.9% *vs.* 49.4%; P<0.01) on visit 3 as compared to baseline. Looking individually, the increased usage was significant only for topical tretinoin (43.0% *vs.* 28.6%; P<0.01) and oral doxycycline (39.6% *vs.* 27.8%; P<0.01). With the increased use of acne creams and antibiotics, there was significant improvement in the overall acne condition (P<0.01) for these patients. The number of patients with moderate to severe acne reduced from 179 (74.3%) at baseline to 36 (23.8%) at visit 3 (P<0.01). The culture status also showed a decline in the number of *C. acnes* isolation from 241 to 58 at end of study.

There was an increase in the proportion of patients who were resistant at visit 3 (40.4%) as compared to baseline (28.5%), but it failed to reach significance (P=0.17). When comparing the minimal inhibitory concentrations (MIC) of each antibiotic at visit 3 with the baseline, a trend towards increase in the MIC was seen with all antibiotics except doxycycline but it was not significant. The maximum increase was seen for erythromycin (65.54+111.78 to 103.40+126.82; P=0.08). Doxycycline showed an overall reduction in the mean MIC at visit 3 (0.57+1.32) as compared to baseline (1.85+17.07) but the difference was not significant.

Out of the 167 patients who tested positive for *C. acnes* at visit 1 and were sensitive to all the antibiotics tested, 134 patients could be taken for resistance analysis at visit 2 and 104 patients at visit 3. Of these, 6 (4.5%) patients turned out resistant at visit 2 and 10 (9.6%) were resistant at visit 3. The 10 patients who were resistant at visit 3 were not resistant at visit 2. 8 of them were still sensitive at visit 2 and 2 were negative for *C. acnes* at visit 2 (Table 3).

Antibiotics	Resistant isolates at visit 2 (n=6)	Resistant isolates at visit 3 (n=10)
Clindamycin	4	10
Erythromycin	5	10
Doxycycline	0	1
Tetracycline	0	1
Minocycline	1	0

Table 3: Resistance patterns of *P. acnes* isolates which were sensitive at baseline but turned resistant at later visits.

At visit 2, 5 (3.7%) were resistant to erythromycin and 4 (3.0%) to clindamycin and 1 (0.7%) to minocycline. At visit 3, all 10 (9.6%) isolates were resistant to erythromycin and clindamycin. One patient (1.0%) was resistant to doxycycline and tetracycline also, in addition to erythromycin and clindamycin (Table 3). Overall, 16 patients (11.6%) who were sensitive at visit 1 were resistant either at visit 2 or visit 3. The most common antibiotic to which they were resistant were Erythromycin (n=15, 10.9%), followed by clindamycin (n=14, 10.1%), doxycycline (n=1, 0.7%), tetracycline (n=1, 0.7%) and minocycline (n=1, 0.7%). One patient was resistant to 4 antibiotics, 13 patients were resistant to at least 2 antibiotics and 15 patients were resistant to at least 1 antibiotic. It was observed that erythromycin and clindamycin resistance occurred concurrently in most of the cases (12 out of 16). There was no significant difference in the current antibiotic use between the resistant and sensitive groups except minocycline which was used more frequently in the patients who harbored resistant strains (12.5%) as compared to those who had sensitive strains (0%, P=0.01) (Table 4). Patients who were negative for *C. acnes* at visit 1 (n=160) were also followed up at 2 months (visit 2) and 4 months (visit 3). Of these, resistance analysis could be done for 131 patients at visit 2 and 47 patients at visit 3.

Previous h/o antibiotic use for acne	Resistant at visit 2 or visit 3 n=16	Sensitive at visit 2 and visit 3 n=122	p-value
Any antibiotic	14 (87.5%)	108 (88.5%)	1

Clindamycin (Topical)	1 (6.3%)	32 (26.2%)	0.12
Erythromycin (Oral)	2 (12.5%)	25 (20.5%)	0.74
Erythromycin (Topical)	1 (6.3%)	7 (5.7%)	1
Doxycycline	10 (62.5%)	72 (59%)	1
Tetracycline	0	0	NA
Minocycline	2 (12.5%)	0 (0%)	0.01
All values are expressed as number and percentage (%).			

Table 4: Resistance patterns of *P. acnes* isolates which were sensitive at baseline but turned resistant at later visits and correlation with previous antibiotic use.

At visit 2, 81 patients (61.8%) remained negative, 34 (26%) patients were sensitive to antibiotics and 16 (12.2%) were resistant to at least 1 antibiotic. A total of 20 patients who had negative cultures at baseline were found to be resistant either at visit 2 or visit 3. Sixteen patients were resistant at visit 2 and six subjects were resistant at visit 3. Resistance was most commonly seen to erythromycin and clindamycin (n=20, 15.2%), followed by doxycycline (n=10, 7.6%), tetracycline (n=6, 4.5%) and minocycline (n=3, 2.3%) (Table 5). The difference in the previous antibiotic use reached significance only at visit 3 where it was found that subjects who harbored resistant strains used doxycycline less frequently than those who had sensitive strains of *C. acnes* (33.3% *vs.* 75%; P=0.02) (Table 6).

Antibiotics	Resistant isolates at visit 2 (n=16)	Resistant isolates at visit 3 (n=6)
Clindamycin	16	6
Erythromycin	16	6
Doxycycline	8	4
Tetracycline	5	3
Minocycline	2	1

Table 5: Resistance patterns of patients who had negative cultures for *P. acnes* at baseline but cultured resistant isolates of *P. acnes* at later visits.

Previous h/o antibiotic use for acne	Resistant at visit 3, n=6	Sensitive at visit 3, n=8	Negative at visit 3, n=33	p-value
Any antibiotic	5 (83.3%)	7 (87.5%)	24 (72.7%)	0.87
Clindamycin (topical)	1 (16.7%)	0	5 (15.2%)	0.64
Erythromycin (Oral)	2 (33.3%)	0	10 (30.3%)	0.19
Erythromycin (Topical)	1 (16.7%)	0	0	0.13
Doxycycline	2 (33.3%)	6 (75%)	8 (24.2%)	0.02
Tetracycline	0	0	0	NA
Minocycline	0	0	2 (6.1%)	1
All values are expressed as number and percentage (%)				

Table 6: Resistance patterns of patients who had negative cultures for *P. acnes* at baseline but cultured resistant *P. acnes* isolates at visit 3 and correlation with previous antibiotic use.

Discussion

Topical and systemic antibiotics have been commonly since a very long time for the treatment of inflammatory acne vulgaris. They improve acne lesions by inhibiting the growth of *C. acnes* and/or their production of pro-inflammatory mediators [3,4]. Although *C. acnes* is known to be sensitive to a wide range of antibiotic classes including clindamycin, macrolides, and cyclines, however the resistant strains of *C. acnes* are gradually increasing worldwide with the rampant use of antibiotics and the patterns vary from one region to another [7,9,12-14,18-22].

Our study showed a *C. acnes* prevalence of 60% which was comparable to the isolation rates of 66.4% by a previous community based study from Singapore in 2007but lesser than a Hong Kong based study (77.4%) and one other from India (65%) [12,18,20]. Much higher prevalence rates were seen in a multicentric study from Europe (94%) [9]. The previous use of antibiotics among acne patients in our study was 49.4% which was comparable with the 48% in the European study [9] but far less than the Hong Kong study [18]. The most common antibiotic used in our study was doxycycline which contrasts with the other two studies mentioned above where clindamycin and erythromycin were the most common antibiotics used [12,18].

There is an evidence for an overall increase in the use of antibiotics for acne in Singapore. The previous use of antibiotics among patients harboring *C. acnes* was 25.2% in the previous community study as compared to 49.4% in our study [1]. With the overall increase in the use of antibiotics among acne patients, the percentage of acne patients carrying *C. acnes* strains resistant to these antibiotics is increasing worldwide and vary from one region to another [7,9,13,14,18-22]. In Singapore, a study carried out in 1999, the antibiotic resistance rate was 11% [13]. In that study, no resistant strains were identified in patients who had not received any antibiotics. Another study in 2007, antibiotic-resistant strains of *C. acnes* increased to 14.9 %, of which, 42% had received antibiotic treatment for acne [12]. Our study showed a resistance rate of 28.5% and the antibiotic use among the patients harboring resistant strains has further increased to 59.7% in our study. However, as compared to other studies, the resistance rates in Singapore are less as compared to 54.8% in Hong Kong and Europe (50.8% to 93.6%) [9,18]. Looking at the high proportion of antibiotic use (92.7%) in the Hong Kong study as compared to 49.4% in our study, the results can be justified. Why resistance rates in Europe was far more than our study, despite having similar rates of previous antibiotic use is not understood. Probably, the increase in resistant strains in the European study could be in part due to the transfer of resistant strains from close contacts.

Similar to our study, erythromycin and clindamycin were the commonest to develop antibiotic resistance in many previous studies [9,12,13,23-27]. These studies also showed combined resistance to erythromycin and clindamycin. Cross-resistance to erythromycin and clindamycin was a common finding in our study. The mechanism underlying erythromycin and clindamycin resistance was elucidated by Ross et al. [28], who identified four phenotypes with cross sensitivity to macrolide, lincosamide and streptogramin B (MLS) antibiotics.

Genetic mutations occur mainly in 23S rRNA, and strains that possess the erm (X) resistance gene are highly resistant to MLS antibiotics. Minocycline resistant strains were detected in Singapore in 2007and the percentage resistance since then (1.7%) has remained constant in our study (1.7%) indicating the lesser propensity of minocycline to develop resistance or an overall reduced frequency of its use in our patients (4.7%) [12]. We could not find any significant difference in the acne severity between patients harboring resistant strains versus those who had sensitive strains of *C. acnes*. Toyne et al. [29] had also found in their cohort that the severity of acne was not linked to resistance.

Patients harboring resistant strains of *C. acnes* were more likely to have received oral erythromycin and oral minocycline in our study. These patients were also more likely to have received topical clindamycin though the difference failed to reach statistical significance (P=0.1). These findings are similar to the European study by Ross et al. [9] which concluded that bacterial resistance is promoted by a previous treatment with MLS antibiotic (azithromycin, erythromycin, clindamycin) and use of topical clindamycin drives resistance to itself and erythromycin. This study also demonstrated that resistance to tetracyclines was more likely when the treatment regimen included any tetracycline, and minocycline was the as the driver of resistance to tetracyclines. On the other hand, Zandi et al. [22] and Sardana et al. [20] did not find any difference any difference in treatment history between resistant and sensitive strains. While Zandi et al. attributed it to shorter period of antibiotic therapy, Sardana et al. attributed the lack of correlation to the mutation based resistant strains which tend to persist.

When patients with sensitive strains were observed over the 4 month follow up period, approximately double the proportion were resistant at 4 months than at 2 months (9.6% *vs.* 4.5%) [30,31]. Almost all of these subjects were on one or other antibiotic at the time of specimen collection. Minocycline was the only antibiotic which was used significantly more by the resistant group supporting the finding by Ross et al. [9] that minocycline serves a selective agent and the driver of resistance.

Although the most common antibiotics to have developed resistance were erythromycin and clindamycin, there was no difference with regards to current antibiotic use of MLS antibiotics between the resistant and sensitive groups. This can be attributed to the short follow up period of 4 months in our study. Evidence exists that the frequency of isolation of resistant strains increases with the duration of antibiotics and in antibiotic naïve patients resistant strains begin to emerge mostly after 12 to 24 weeks of therapy [14,32]. It is also possible that the resistant isolates in many of these patients could have been obtained from their close contacts harboring resistant strains [9].

In patients who turned resistant at visit 3 from negative culture results at baseline, doxycycline appeared to have a statistically significant decreased usage than those with sensitive strains. It is important to note that doxycycline, despite being used very commonly had a lesser propensity to develop resistance. This could be attributed to the fact that topical cyclines are not used for treatment in acne which could be the reason for the reduced prevalence of cycline resistant strains [21,33-37].

Conclusion

Our results suggests that doxycycline despite being the most frequently used antibiotic overall, has lesser propensity to develop resistance. Minocycline appears to be the most selective agent among the cyclines. Previous history of treatment with erythromycin, minocycline and also clindamycin tends to influence the development of antibiotic resistance. Resistance of *C. acnes* is common to erythromycin and clindamycin, as is the cross resistance between them which is mostly related to their frequent topical use. Combining topical antibiotics with zinc acetate or gluconate or benzoyl peroxide is a helpful strategy to inhibit the growth of pre-existing erythromycin-resistant *C. acnes* and helps to prevent the emergence of resistant strains which occurs when the antibiotic is used alone. It is important that the physicians be aware of the increasing antibiotic resistance, obtain a good history of previous antibiotic usage and be vigilant when prescribing antibiotics for acne.

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