Efficacy of octenidine dihydrochloride and 2-phenoxyethanol in the topical treatment of inflammatory acne

S. Mayr-Kanhäuser, B. Kränke, and W. Aberer

ABSTRACT

Background: With the increase in antibiotic-resistant strains of microorganisms in acne lesions, the search for alternative treatment methods has become important. We studied the efficacy of a combination of the antiseptic substances octenidine dihydrochloride and 2-phenoxyethanol (O/P) in mild to moderate inflammatory acne vulgaris.

Methods: Thirty patients were instructed to apply O/P once or twice daily for a 6-week treatment period. Determination of efficacy included the numerical documentation of inflammatory and non-inflammatory lesions within defined regions of the face by the investigator, and photodocumentation of the clinical picture as well as the fluorescence pattern under Wood's light.

Results: Twenty-four patients completed the study. The number of papules and pustules decreased more than 50% in seventeen and nineteen patients, respectively. Acne lesions worsened in only one patient. Mild adverse reactions (erythema, burning, and scaling) were seen in two patients. Therefore, O/P was highly effective in treating inflammatory lesions of facial acne, but there was no essential efficacy in the non-inflammatory primary acne lesions.

Conclusion: Topical O/P is a good and cost-effective alternative in the treatment of mild to moderate inflammatory acne lesions and may allow reduced application of anti-acne antibiotics to prevent development of resistance.

KEY WORDS

acne, antibiotic resistance, octenidine dihydrochloride, 2-phenoxyethanol

Introduction

Acne vulgaris is a worldwide common skin disorder of the sebaceous follicles, which are special pilosebaceous units located mostly on the face, chest, and back. Because the lifetime prevalence is nearly 100%, most adolescents develop acne lesions differing only in the severity of expression. Up to 30% of the individuals involved

Note: SMK was in clinical charge of the patients, and all authors designed the report presented, prepared and revised the manuscript, and approved the final version.

Table 1. Patient characteristics;

Patient (no., initials, sex, age)	**Inclusion** com/pap/pust	**Follow-up 1** com/pap/pust	**Follow-up 2** com/pap/pust	**Follow-up 3** com/pap/pust
1. S.M. F 16 yrs	82 / 15 / 5	76 / 10 / 5	45 / 7 / 2	–
2. S.G. M 22 yrs	17 / 17 / 8	10 / 3 / 1	5 / 1 / 1	–
3. O.R. M 17 yrs	97 / 15 /12	91 / 9 / 7	80 / 3 / 2	–
4. F.S. F 18 yrs	17 / 9 / 9	12 / 8 / 4	4 / 3 / 1	–
5. S.I. F 15 yrs	60 / 25 / 17	46 / 9 / 10	28 / 5 / 4	–
6. R.J. F 22 yrs	31 / 8 / 10	19 / 17 / 7	10 / 8 / 0	–
7. E.F. M 20 yrs	115 / 12 / 3	85 / 9 / 0	115 / 5 / 0	–
8. K.A. F 17 yrs	72 / 24 / 45	36 / 8 / 5	37 / 8 / 1	–
9. L.M. F 18 yrs	28 / 29 / 14	21 / 26 / 8	19 / 27 / 7	11 / 13 / 4
10. R.M. F 23 yrs	76 / 19 / 6	55 / 12 / 4	33 / 4 / 2	–
11. R.A. F 22 yrs	48 / 17 / 11	56 / 8 / 0	40 / 6 / 0	–
12. N.W. M 18 yrs	56 / 12 / 12	37 / 9 / 0	15 / 4 / 0	–
13. P.L F 16 yrs	58 / 12 / 3	60 / 5 / 3	70 / 12 / 7	70 / 15 / 9
14. W.H. F 23 yrs	170 / 14 / 11	170 / 15 / 2	150 / 6 / 0	–
15. E.T. M 17 yrs	60 / 13 / 13	80 / 13 / 8	70 / 12 / 7	–
16. R.A. M 16 yrs	26 / 18 / 27	27 / 19 / 15	31 / 8 / 6	–
17. W.O. M 18 yrs	110 / 16 / 10	90 / 14 / 7	80 / 12 / 3	–
18. G.M. F 17 yrs	70 / 19 / 11	70 / 16 / 7	60 / 9 / 6	–
19. H.M. M 15 yrs	120 / 24 / 27	120 / 10 / 25	95 / 9 / 11	–
20. L.U. F 19 yrs	180 / 18 / 9	160 / 22 / 4	87 / 10 / 4	–
21. E.B. F 20 yrs	38 / 7 / 11	28 / 8 / 2	18 / 3 / 5	–
22. K.T. F 15 yrs	95 / 9 / 27	75 / 14 / 20	75 / 4 / 5	–
23. B.W. M 23 yrs	40 / 5 / 7	35 / 8 / 3	15 / 2 / 0	–
24. R.M F 22 yrs	76 / 19 / 6	74 / 12 / 6	53 / 17 / 6	49 / 4 / 2

Abbreviation: com = comedones, pap = papules, pust = pustules; F = female, M = male; Follow-up 1 after 2–3 weeks, Follow-up 2 after 6 weeks, Follow-up 3 after 8 weeks of therapy.

require medical treatment, and systemic as well as topical antibiotics are the agents most commonly used in the therapy of inflammatory lesions such as papules or pustules (1). Unfortunately, a significant and worrying increase in the number of antibiotic resistant strains of *P. acnes* has been reported in the last decade (2–4). Moreover, the lowest prevalence of propionibacterial resistance can be found in young (10- to 14-year-old) patients, indicating an important role of previous treatments with antibiotics in older acne patients (5). As a result, there is a need for new non-antibiotic treatment of acne.

Methods

Study objective

The purpose of this pilot study was to evaluate the efficacy of monotherapeutically applied Octenisept® (octenidine dihydrochloride, 2-phenoxyethanol, Schülke & Mayr, Germany), a topical skin antiseptic marketed since 1988, in patients with mild to moderate inflammatory acne.

Study design

The study was designed as a single-center, prospective, open-labeled clinical trial. To be included, patients had to present with more than 15 non-inflammatory lesions (white and black comedones) and more than 5 inflammatory lesions (papules, pustules and papulopustules) on their faces (6). Exclusion criteria were nodulocystic lesions, fewer than 5 inflammatory lesions, systemic antibiotic or retinoid therapy within the last 6 months, and manifestations of other cutaneous diseases of the face. Before the study started, all the patients included gave their written informed consent. At start of the study, the precise anamnestic data were evaluated including former therapies, skin type classification, atopy scoring, allergies, and medication including oral contraceptives.

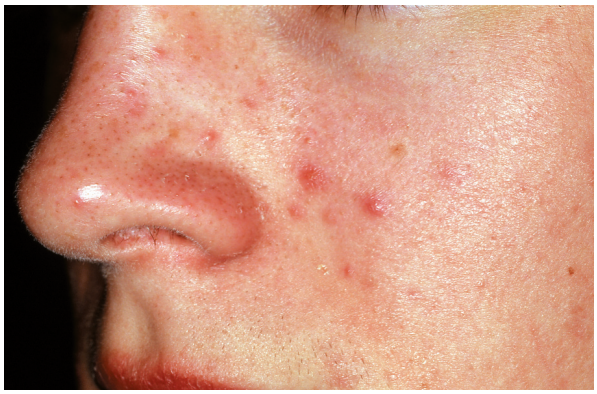


Figure 1a. Comedones and inflammatory acne lesions on the left cheek (inclusion phase).

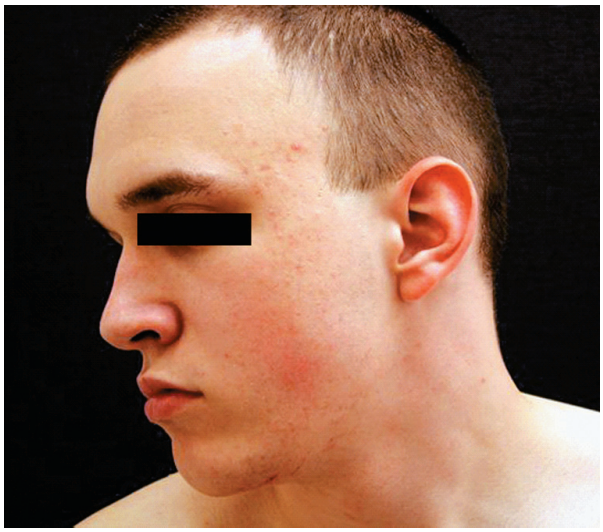


Figure 1b. Same patient as in 1a at the 6-week follow-up assessment.

Efficacy parameters

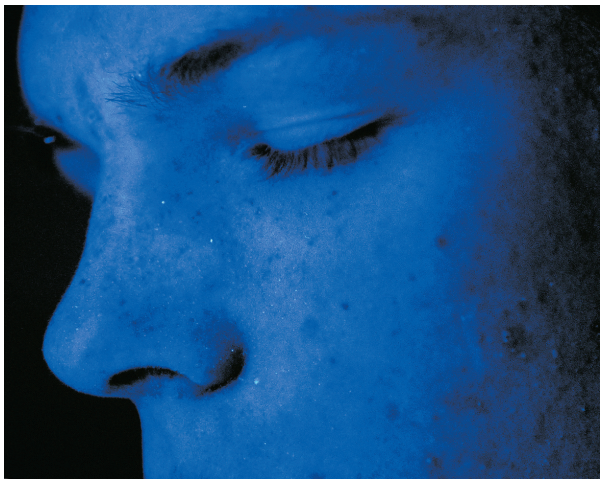
Photodocumentation and fluorescence photography, currently the best tool in the clinical assessment of acne, was performed; the investigator also counted the inflammatory and non-inflammatory lesions. Figures 1a and b (7–9). The number of lesions within defined regions of the face (forehead, and left and right cheeks including the adjacent part of the nose and chin) were documented. Because the punctate fluorescence detected with Wood's light examination corresponds to coproporphyrin III and protoporphyrin IX produced by *Propionibacterium acnes,* photodocumentation of this phenomenon was useful to quantify and evaluate the efficacy of acne treatment protocols (10). Figures 1a and b.

Patients were instructed to clean their faces thoroughly first once a day at bedtime, and if well tolerated twice a day with O/P. In patients with atopy, the mode of application was determined as once daily in order to avoid an (hypothetical) irritant reaction. In facial regions with multiple inflammatory lesions they were instructed to apply a compress with O/P for 1 to 2 minutes twice a day. No other local or systemic acne therapy was allowed, with the exception of a skin-care product (Diprosicc®, AESCA, Austria). The efficacy and cutaneous tolerance of the therapy were assessed and documented by the investigator with the same methods 2 to 3 weeks and 5 to 6 weeks after initiation of treatment. If there was a missing response within this period, a final examination was performed after 8 weeks.

Tolerability

All adverse events reported during the trial were recorded.

Figure 2a. Decrease of punctate fluorescence in Wood's light before therapy.



Picture 2b. Decrease of punctate fluorescence in Wood's light after therapy, demonstrating treatment efficacy.

Results

30 Caucasian patients with acne comedonica et papulopustulosa of the face (18 females, 12 males; age range 14 to 23 years) were included. 24 (80%) patients completed the study and 6 (20%) discontinued for the following reasons: 1 left because of visible signs of irritation due to the antiseptics, a 14-year-old girl left because she developed acne conglobata (exploration of the hormones discovered abnormalities), and 4 were lost to follow-up. In 3 (10%) patients there was no response after 6 weeks, and 2 of them showed delayed improvement after 8 weeks of treatment. In 1 patient the acne lesions worsened. In the 21 (70% of the initial study cohort) patients that improved within the treatment period, the number of pustules decreased more than 50% in 19 (63% of the initial study cohort, 83% of the patients that improved), and this increased to 21 after 8 weeks. The papules decreased in 17 and 19 patients (57% and 77%, respectively). Nine (30% and 41%, respectively) patients showed a more than 50% reduction of comedones. (Table 1)

Safety

Two patients developed irritant reactions such as erythema, burning, and scaling, and one of them discontinued as mentioned above. No other adverse effects were observed.

Discussion

For decades topical therapy with antibiotics has been the first choice in treating inflammatory acne, and in the 1970s many experts believed that *P. acnes* was incapable of developing resistance (11). Because antimicrobial therapy is only palliative – acne is not an infection in the traditional sense, and acne lesions usually persist for some years during the second decade of life – the majority of patients need several courses of treatment before the disease spontaneously regresses. Unfortunately, numerous studies have recently raised the issue of increased bacterial resistance in acne patients (2–4, 12, 13), and the likelihood of overgrowth of resistant *P. acnes* increases with the duration of antibiotic therapy (14, 15). Actually, the proportion of patients carrying strains resistant to the commonly used erythromycin, clindamycin, and tetracycline is reported to range from 34.5% to 64% (4).

Octanidine is well documented to have a very good safety profile (no resorption when applied on wounds, mucous membranes, etc.) and is highly effective against a wide range of microorganisms including *MRSA, Staphylococcus epidermidis, Streptococcus pyogenes, Proteus mirabilis, Klebsiella pneumoniae, E. coli,* and *Pseudomonas aeruginosa* (16, 17). Moreover, it has a remnant effect in microbial skin decontamination, so we decided to employ O/P in the treatment of mild to moderate inflammatory acne. The results of this study show that the combination of octenidine dihydrochloride and 2-phenoxyethanol is highly effective in treating inflammatory acne lesions (papules, pustules, and papulopustules) within 6 to 8 weeks. However, the topically-applied antiseptic evaluated does not markedly reduce non-inflammatory comedones. Because the intensity of fluorescence is known to be proportional to the amount of *P. acnes* (18), the applied solution seems to be effective against the *Propionibacterial* strains. Other mechanisms by which the fluorescence could be suppressed, such as destruction of the fluorescence-inducing porphyrins or decreased production of porphyrins by living *P. acnes* organisms, are less probable with regard to these antiseptics (19). Even if the duration of treatment phases and the time points of efficacy assessment differ in most topical treatment studies, the results of our study are solid when compared with published data. The topical retinoids currently used effectively reduce the number of comedones and inflammatory lesions in the range of 40% to 70%, while topically applied antimicrobials like clindamycin, erythromycin, tetracycline, and benzoyl peroxide attain reduction of lesions from 26% to 85% (20).

Limitations of our pilot study include the absence of blinding, the limited number of participants, and concentration on facial acne.

In conclusion, our open-labeled prospective pilot study showed that topically applied antiseptic therapy with a combination of octenidine diydrochloride and 2-phenoxyethanol can be an effective alternative for the treatment of mild to moderate inflammatory acne. Moreover, it is an extremely cost-effective treatment – the cost per patient for the trial period was 10.05 (about UK £7), which is less than 1% of the amount that patients are willing to accept and pay as found by Ozolins et al. (21) – and therefore seems to be an adequate alternative to established antibiotics. Furthermore, the preferential use of local antiseptics, given alone or in combination with topical antibiotics, will help decrease resistance development.

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