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The Efficacy of Topical Solution of 0.3% Ciprofloxacin in Treatment of Mild to Moderate Acne Vulgaris

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Abstract

Background: Acne vulgaris is a very common disorder affecting virtually every adolescent at some point in time. Topical treatment of acne involves the use of retinoids and antimicrobials. Antimicrobials reduce *P. acne* population and are effective for treatment of inflammatory lesions. We evaluated the efficacy and safety of topical ciprofloxacin solution and compared it with topical erythromycin solution.

Methods: The study was a prospective single-blind clinical trial. One hundred patients with mild to moderate acne were enrolled. The patients were randomly treated with topical application of 0.3% ciprofloxacin or 4% erythromycin solutions. For a six week period, they were visited every two weeks. Acne severity index (ASI) was calculated in each visit and recorded.

Results: Ninety-three patients completed the study, 50 patients in the ciprofloxacin and 43 in the erythromycin groups. Irritation was generally mild for both treatments and no discontinuation was reported because of adverse effects. There was no statistically significant difference between the two treatment groups in reduction of comedons or papules but reduction of pustules was greater in ciprofloxacin treatment group after 4 weeks. ASI was reduced in the two groups but in ciprofloxacin treated patients, this reduction was more significant at all follow up visits.

Conclusion: The results of this study indicate that topical solutions of erythromycin and ciprofloxacin were effective in treating mild to moderate acne vulgaris and both were well-tolerated by the patients. Ciprofloxacin solution produced greater reduction in pustule counts and ASI, during the six week period of twice-daily application. This novel modality may have an important potential role in rotational topical therapy of inflammatory acne lesions.

Keywords: Ciprofloxacin; Acne vulgaris; Therapy; Topical

Introduction

Acne vulgaris is a very common disorder affecting virtually every adolescent at some point in time.[1] Acne is a disorder of the pilosebaceous follicle; common features include increased sebum production, follicular keratinization, colonization by *Propionibacterium acnes* (*P. acnes*) and localized inflammation.[2] Ideal treatment must affect all of these pathogenic mechanisms. There is not such ideal therapy; therefore, clinicians usually combine several topical and systemic agents to achieve best results. The most widely used topical drugs for acne treatment are benzoyl peroxide, retinoids, topical antibiotics and azelaic acid either as monotherapy or in combination.[3]

Treatment is more effective with a combination of the antimicrobial with topical retinods than if either medication is used alone. Antimicrobials reduce *P. acnes* population and are effective for treatment of inflammatory lesions. Commonly used topical antimicrobials include erythromycin, clindamycin and benzoyl peroxide. Other antimicrobials used in acne therapy include sulfacetamide, sulfacetamide-sulfur combinations, metronidazole and azelaic acid.[4] Systemic therapy is added to topical therapy in cases with more severe involvement.[5]

Neither of the topical treatments is ideal. The retinoids cause irritant contact dermatitis and benzoyl peroxide causes allergic contact dermatitis. Such side

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effects limit the use of such treatments. Topical antimicrobials may cause microbial resistance. In recent years, the issue of antibacterial resistance has become more prominent, especially with concerns that *P. acnes* can transfer antibacterial resistance to other bacteria within the resident skin flora.[1] Ciprofloxacin is a member of quinolone family and represents a particularly important therapeutic advance, since it has a broad antimicrobial activity and is effective after oral administration for the treatment of a wide variety of infectious diseases. It has relatively few side effects and microbial resistance to their action does not develop rapidly.[6]

Ophthalmologists have administered ophthalmic drop of ciprofloxacin since several years ago for treatment of bacterial conjunctivitis safely and effectively. Ciprofloxacin hydrochloride (CILOXAN) is available as 0.3% solution for ophthalmic use and is indicated in cases with conjunctivitis and keratitis.[7] The 0.3% ciprofloxacin solution was not used in dermatology before. We used it as a novel topical therapy for acne and compared its efficacy and safety with 4% topical erythromycin solution.

Materials and Methods

One hundred patients (56 female and 44 males) with mild to moderate acne that signed informed consent were included in this study. No other cutaneous disease was present on the face. The exclusion criteria included any indication for systemic antibiotics, e.g. truncal acne or severe cases (nodulocystic acne), consumption of a systemic antimicrobial during the study or four weeks before it, consumption of any topical agent for acne during the study or 2 weeks before, pregnancy, breast-feeding and unwillingness for the use of appropriate contraceptive methods during the study. Randomization was performed by coin flipped manner. A clinician was responsible for randomization and prescription of the drugs. The patients were randomly treated with topical application of A or B solution, twice daily. Effective ingredients of A and B solutions were 0.3% ciprofloxacin and 4% erythromycin plus 1.2% zinc acetate, respectively. The vehicle for both solutions was 70^0 ethanol plus 5% propylene glycol that was added to act as a penetration enhancer. For preparation of ciprofloxacin solution, the pharmacist used ciprofloxacin hydrochloride monohydrate (C17H18FN3O3, HCL, H2O) available as a powder and soluble in diluted acetic acid, which should be protected from light.[2] Containers of all solutions were identical dark 100 ml bottles.

The patients were instructed to wash their faces with an antiseptic soap which included 1% trichlocarban and applied their solution with finger tip to all areas of the face after shaking the bottle well twice daily. The patients were assessed at the baseline and after 2, 4 and 6 weeks of treatment by the same clinician. The information about patient, e.g. name, address, age, and counts of lesion type such as comedons, papules and pustules and any side effect, e.g. redness, erythema, pruritus and xerosis were recorded in related forms. Acne severity index (ASI) was calculated in each visit and registered. The formula of ASI was 2 × pustules + 1 × papules + comedones × 1/4). Statistical analysis was performed using independent t test with SPSS soft ware (version 11.5, Chicago, IL, USA).

Results

Ninety-three patients completed the study, 50 patients in the ciprofloxacin and 43 in the erythromycin groups. Of the seven patients who did not complete the study, three left for acne flare, two for concurrent infection that necessitated consumption of oral antibiotics and two were lost in follow-up. They were all in erthromycin treated group. Male to female ratio was 38/55. The mean age in the ciprofloxacin group was 21.9±6.48 and in the erythromycin group, 21.7±6.1. The mean baseline lesion count, age and sex did not differ significantly between the two treatment groups. There was a gradual reduction in the counts of non-inflamed and inflamed lesions in both groups.

There was no statistically significant difference between the two treatment groups in reduction of comedons or papules (Table 1 and 2) but reduction of pustules was greater in ciprofloxacin treatment group, being statistically significant after four weeks (P=0.01; Table 3). Although ASI was reduced in the two groups but in ciprofloxacin treated patients, the reduction was more significant after six weeks (Table 4).

The patients were assessed based on reduction of ASI compared with baseline condition. Good response was considered when the patients achieved 71-100% recovery, 36-70% as moderate response and 0-35% as poor response. The patients treated by ciprofloxacin solution achieved moderate response after four weeks but response to treatment was poor in erythromycin group even after six weeks (Table 5).

Table 1: Comparisons of the comedon counts in different treatment groups in two weeks intervals.

Treatment group	First visit comedon counts (Mean±SD)	Second visit comedon counts (Mean±SD)	Third visit comedon counts (Mean±SD)	Forth visit comedon counts (Mean±SD)
Ciprofloxacin solution	10.8±4.30	9.08±3.20	7.45±3.00	6.45±3.10
Erythromycin solution	10.2±4.30	8.67±3.30	7.20±3.20	6.3±3.30
P value	0.57	0.56	3.71	0.82

Table 2: Comparisons of the papule counts in different treatment groups in two weeks intervals.

Treatment group	First visit papule counts (Mean±SD)	Second visit papule counts (Mean±SD)	Third visit papule counts (Mean±SD)	Forth visit papule counts (Mean±SD)
Ciprofloxacin solution	5.96±3.00	4.58±2.10	3.81±2.10	3.20±1.90
Erythromycin solution	4.55±1.80	3.93±7.10	3.30±1.70	1.30±2.80
P value	0.007	0.11	0.22	0.97

Table 3: Comparisons of the pustule counts in different treatment groups in two weeks intervals.

Treatment group	First visit pustule counts (Mean±SD)	Second visit pustule counts (Mean±SD)	Third visit pustule counts (Mean±SD)	Forth visit pustule counts (Mean±SD)
Ciprofloxacin solution	4.76±2.30	3.77±1.90	3.04±2.04	2.97±2.20
Erythromycin solution	5.81±3.30	4.55±1.90	4.27±2.50	4.16±3.40
P value	0.09	0.06	0.01	0.04

Table 4: Comparisons of the Acne Severity Index (ASI) in different treatment groups in two weeks intervals.

Treatment group	First visit ASI (Mean±SD)	Second visit ASI (Mean±SD)	Third visit ASI (Mean±SD)	Forth visit ASI (Mean±SD)
Ciprofloxacin solution	18.01±6.60	13.90±5.50	11.44±6.00	10.02±6.70
Erythromycin solution	18.94±6.90	15.23±4.70	13.72±5.80	13.86±8.60
P value	0.57	0.29	0.11	0.04

Table 5: Reduction of Acne Severity Index (ASI) compared with the baseline condition in different treatment groups in two weeks intervals.

Treatment duration Reduction of ASI	Two weeks %	Four weeks %	Six weeks %
Ciprofloxacin treated group	22.8	36.5	44.4
Erythromycin treated group	19.6	27.6	26.8

Irritation was generally mild for both treatments and no discontinuation was reported because of adverse effects. There were two reports of xerosis, one case with erythema and one case with stinging sensation in ciprofloxacin treated group versus five cases with erythema and one report of stinging in the erythromycin treated group.

Discussion

The results of this study indicated that topical solutions of 4% erythromycin and 0.03% ciprofloxacin were effective in treating mild to moderate acne vulgaris and both were well-tolerated by the patients. Ciprofloxacin solution produced greater reduction in pustule counts and ASI, during the six week period of twice-daily application.

Erythromycin is a well established and effective topical antibiotic in acne therapy since three decades ago.[8,9] Our study showed that erythromycin is still an effective and safe topical therapy in acne. One of the major setbacks in the use of topical antibiotics has been the dramatic increase in bacterial resistance over

the past 20 years. Antibiotic-resistant strains of *P. acne* are found worldwide; therefore, combination therapies of topical antibiotics (e.g. with benzoyl peroxide, topical retinoids or azelaic acid) are now favored, because this reduces the existing resistant. *P. acne* counteracts the selection of new, resistant *P. acne* and reduces the risk of colonization with resistant *Staphylococcus aureus*.[10] We added zinc acetate to the solution of erythromycin as combination therapy due to its comedolytic effects.[5]

Ciprofloxacin is a member of quinolone family whose mode of action is via inhibition of DNA synthesis with broad spectrum activity that covers both gram positive and gram negative bacteria.[11] In dermatology, systemic ciprofloxacin is used in severe infections in immunocompromised patients, gram-negative folliculitis, rhinoscleroma, cutaneous anthrax, chancroid and genital chlamydial infections.[3] The side effects of systemic quinolones include CNS toxicity, upper GI tract reactions, photosensitivity, skin rash, pruritus, fever, urticaria, anaphylactic reaction, photo-onycholysis, lichenoid drug eruptions, vasculitis and fixed drug eruption. Systemic ciprofloxacin may cause Stevens-Johnson syndrome or TEN and bullous pemphigoid.[3,12]

In contrast with systemic form, topical ciprofloxacin has fewer side effects and is administered in cases with bacterial conjunctivitis even in children. Ciloxan ophthalmic solution is approved by FDA for the treatment of infections caused by specific microorganisms in the conditions of corneal ulcers and conjunctivitis. We found only mild and transient side-effects due to ciprofloxacin solution in four patients (8%) versus six patients in erythromycin treated group (14%).

In 1992 Vogt studied the antibacterial activity of the topical quinolones against bacteria commonly found in acne vulgaris in vitro.[13] Our study was in vivo with practical clinical importance in contrast with the basically oriented study of Vogt. However, both studies had similar results and showed that topical quinolons were more effective than erythromycin in acne vulgaris.

Langer showed that clindamycin plus benzoyl peroxide and erythromycin plus zinc acetate solution are both effective treatments for acne but clindamycin plus benzoyl peroxide has an earlier onset of action that should improve the patient compliance.[14]

Our study is the first clinical trial about the effectiveness and tolerance of ciprofloxacin solution in acne treatment. Both pustule counts and ASI showed a better degree of efficacy with ciprofloxacin than erythromycin solution. The risk of side effects was lower in ciprofloxacin treated patients.

Some bias occurred in this study because of the single–blind design. If we performed the study as double or triple blind design, we could decrease the bias. The blood concentration of ciprofloxacin was not measured and we did not perform any bacterial culture from the pustular lesions. In spite of the above-mentioned biochemical and microbiological limitations, this study introduces a new, safe and cost-effective topical therapy for acne.

This study indicates that ciprofloxacin solution may begin a new era of treatment with topical antimicrobials in acne vulgaris that is safe, well-tolerated and cost-effective.

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