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Treatment of Acne Vulgaris Using Topical and Oral Ciprofloxacin in Comparison with Topical Clindamycin and Oral Doxycycline

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Abstract: ***There are many topical therapies that have been used in the treatment of mild to moderate acne vulgaris, while in moderate to severe acne systemic therapies are recommended in addition to the topical remedies. The aim of this study is to assess the efficacy and safety of oral plus topical ciprofloxacin solution 1.5% in the treatment of moderate acne vulgaris in comparison with topical clindamycin solution 1.5% plus oral doxycycline. This single-blind comparative therapeutic clinical trial was conducted in the Department of Dermatology and Venerology-Baghdad Teaching Hospital from February 2017 to March 2018, consisted of seventy one patients with moderate acne who were divided into two groups: Group A used topical ciprofloxacin solution 1.5% twice daily for 8 weeks plus 500mg ciprofloxacin tablet twice daily for the first two weeks, then once daily for the remaining 6 weeks (total 8 weeks), while Group B used topical clindamycin solution 1.5% twice daily plus 100 mg doxycycline capsule in the same manner. Full clinical assessment was carried out. Scoring system was done every two weeks till the end of the therapy and four weeks after the cessation of therapy to evaluate the improvement and to report any topical and systemic side effects. Sixty two patients with moderate acne vulgaris completed the course of treatment, thirty one patients in each group, their ages ranged from 17-26 (19.3 ± 1.9) years and for group A, group B as follow: 19.5 ± 2.3, 19.1 ± 1.5 years respectively, nine (12.3%) patients did not complete the study. Both topical ciprofloxacin solution plus oral ciprofloxacin and clindamycin solution plus oral doxycycline cleared the lesions in moderate acne within 8 weeks and when the results of the two groups compared with each other there was no statistical difference. In conclusion Topical ciprofloxacin solution plus systemic ciprofloxacin are as effective as topical clindamycin solution plus systemic doxycycline in the treatment of moderate acne vulgaris.***

Keywords: Ciprofloxacin, Doxycycline, Acne Vulgaris

1. Introduction

Acne vulgaris is a major health problem among youth and although it is self limiting disease but in many cases if left without treatment cause scarring which has psychological and cosmetical impacts on the patients [1]. The main pathophysiological mechanisms of acne include: hyperkeratinization of pilosebaceous follicles, amplified activity of sebaceous glands and increased bacterial colonization in the pilosebaceous units as well as perifollicular inflammation [2]. Antimicrobial reduce *P. acnes* population and are effective for treatments of inflammatory lesions. Topical antimicrobials like erythromycin, clindamycin and benzoyl peroxide were used mainly for the treatment of mild to moderate acne while systemic therapy is added to topical therapy in cases with more severe involvement [3]. Ciprofloxacin is a member of quinolone family, a second generation floroquinolone antimicrobial and it is a bactericidal drug acts by inhibiting the action of bacterial topoisomerase II and IV during bacterial growth and reproduction. It has broad spectrum activity that covers both gram positive and gram negative bacteria. [4,5,6].

Because DNA gyrase is a bacteriospecific target for antimicrobial therapy, cross resistance with other more commonly used drugs is rare[6]. It has been found that ciprofloxacin is potentially capable of reducing fibrosis through reduction of collagen synthesis or increased matrix metalloproteases (collagenases) and thus might has additional effect in the treatment of acne scars.So it represents new advance in acne treatment[7,8,9]. So the aim of the present work is to evaluate the efficacy of topical ciprofloxacin solution plus systemic ciprofloxacin in comparison with topical clindamycin solution plus systemic doxycycline in the treatment of moderate acne vulgaris.

2. Patients and Methods

This single-blind comparative therapeutic clinical trial conducted in the Department of Dermatology and Venerology in Baghdad Teaching Hospital from February 2017 to March 2018. The total number of seventy one patients with moderate acne vulgaris on the faces were enrolled in this study. Full history was taken from each patient including: age, sex, duration of disease, previous treatment and ensured that every patient had stopped any systemic and topical treatment at least 2 months before starting the present therapy.

Close physical examination was done to evaluate the severity of acne. Scoring the severity of acne was determined according to the following rules [10]:

a) Mild acne in which the count of pustules is less than 20 and the count of papules is less than 10.
b) Moderate acne in which the count of pustules is ranging between 20-40 and the count of papules ranging between 10-30 papules.
c) Severe acne in which the count of pustules is more than 40 and the count of papules is more than 30.

Comedonal, severe and nodulo-cystic acne, patients aged 16 years and less, pregnant and lactating females, patients with immunosuppression conditions, patients on systemic drugs

that induced acneiform eruption and patients with post-epilation acne, acne cosmetica were excluded from this study. Formal consent was taken from each patient after full explanation of nature of the disease, course, treatments, prognosis and its complications, the target of the present work regarding the drug, its efficacy, side effects, the method and duration of treatment and follow up. Also, ethical approval was performed by the Scientific Council of Dermatology and Venereology-Iraqi Board for Medical Specializations. Color photographs for each patient were performed at baseline, at 2 weeks, 4 weeks, 8 weeks and 12 weeks. Frontal, right and left views were taken using Sony-digital, high sensitivity, 12.1 megapixel camera in the same place with fixed illumination and distance.

The 36 patients in group A were treated with topical ciprofloxacin solution 1.5% plus systemic ciprofloxacin in the form of oral tablets [(Sarf.)^{R} Produced by: Julfur-Gulf pharmaceutical industries, Ras Al-Khaima, U.A.E, 500mg] and asked to apply the solution twice daily for two months plus oral ciprofloxacin tablets twice daily for the first two weeks, then once daily for the remaining 6 weeks (total 8 weeks). The clinical evaluation was done every two weeks till the end of the two months. Then the patients were instructed to stop the use of the treatment to be re-evaluated again after four weeks period free of therapy. The assessment carried out by counting the inflammatory lesions (papules and pustules) depending on the scoring and watching for any side effects.

Group B included 35 patients treated with topical clindamycin solution 1.5% plus systemic doxycyclin in the form of oral capsules [(MEDOMYCINE. MEDOCHEMIE-CYPRUS)^{R} 100mg as HCL].

The method of the treatment and follow up were done in the same way as for group A.

Statistical analysis were done using SPSS version 19 (Statistical Package for Social Sciences). Comparison between the two groups done by using independent sample t-test. Comparison before and after treatment in each group was done by using paired t-test, comparison of the patient response to treatment in the two groups done by using chi-square, and P-value < 0.05 was considered as level of significance. F-test (ANOVA) was applied to measure the significance differences between and within groups.

3. Results

Seventy one patients included in this study. Sixty two patients completed the course of treatment, while 9 (12.3%) patients did not complete the treatment, one (1.3%) in group A because of severe nausea and vomiting and 8 (10.9%) patients considered defaulted for unknown reason (4 from group A and 4 from group B), their ages ranged from 17-26 years with a mean ± SD of 19.3± 1.9 years. Thirty one patients in Group A, their mean ages 19.5 ± 2.3, 19 (61.3%) females and 12 (38.7%) males, female to male ratio 1.6:1. Thirty one patients in group B, their mean ages 19.1 ± 1.5, 15 (48.4%) females and 16 (51.6%) males, female to male ratio 0.8:1.

In both groups, the means of inflammatory lesion counts including papules and pustules within each group had been reduced statistically significant at each visit when compared to the baseline starting from the second visit (after two weeks) in group A and in group B (Table 1).

There were no significant differences between the two groups in the total means of the inflammatory lesions at the baseline and at each visit and there is no relapse rate after the stopping of the treatment (Table2).

Regarding group A three (9.6%) patients had gastrointestinal upset, one (3.2%) patient had headache, and one (3.2%) patient had dizziness plus burning sensation, while in group B five (16.1%) patients had gastrointestinal upset and three patients (9.6%) had burning sensation.

Table 1: The mean ± SD of papules and pustules counts within the groups

	1st visit (before therapy)	2 wks	4 wks	8 wks	ANOVA	P- value
Doxycycline						
Papules	6.55±5.42	4.42±4.72*	3.35±4.01*	2.84±4.27*	3.90	0.0105
Pustules	20.84±4.73	13.58±5.61*	10.65±4.94*	8.26±6.39*	31.02	0.000
Total	27.39±4.67	18.00±6.55*	14.00±6.34*	11.10±8.17*	36.42	0.000
Ciprofloxacin						
Papules	12.23±7.73	6.58±7.14*	5.61±6.90*	5.55±7.30*	5.89	0.000
Pustules	20.97±6.63	10.84±6.30*	9.06±5.58*	7.10±6.33*	30.56	0.000
Total	33.19±7.71	17.42±11.45*	14.68±10.32*	12.65±12.10*	24.41	0.000
*significantly different from the 1st visit (p<0.05)						

Table 2: The total mean difference (papules and pustules) between the 2 groups at each visit

	Group A Mean ± SD	Gross reduction Rate	Group B Mean ± SD	Gross reduction rate	t-test	P-value*
(1st visit)	30.1±7.7	41.86%	27.3±4.6	40.65%	3.58	0.08
(2 wks)	17.4±11.4		18±6.5		0.24	0.80
(4 wks)	14.6±10.3		14.0±6.3		0.31	0.75
(8 wks)	12.6±12.1		11.1±8.1		0.59	0.55
(4 wks after R)	11.7±10.5		10.2±7.7		0.63	0.53

*p-value not significant > 0.05

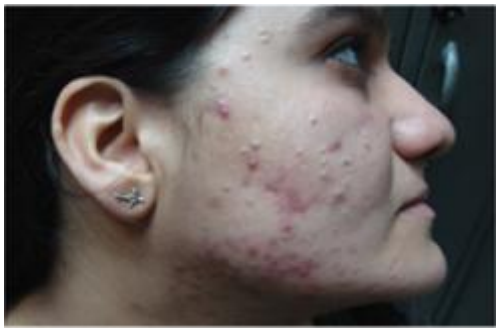

Figure 1: Patient with moderate acne vulgaris before treatment

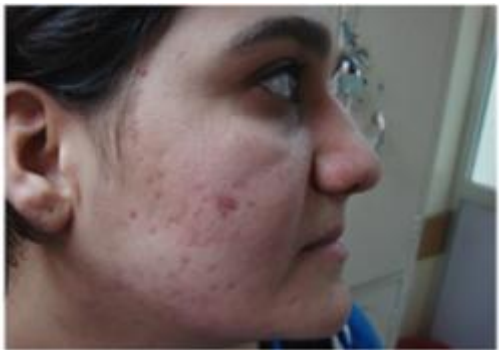

Figure 2: Patient with moderate acne vulgaris after treatment

4. Discussion

Acne vulgaris although it is self limiting disease but could be associated with scarring especially in patient with moderate and severe acne. Accordingly topical therapy like benzoyl peroxide, azelaic acid, retinoic acid, erythromycin were used in the treatment of mild and moderate acne while in severe acne systemic therapies include oral antibiotics such as tetracycline, erythromycin, Trimethoprim, oral retinoic acid and hormonal therapy were recommended in addition to topical therapies[11,12,13].

Doxycycline has been used as systemic therapy in the treatment of acne and proved its effectiveness [14,15].

In the present study ciprofloxacin has been taken as a systemic therapy in combination with topical ciprofloxacin solution in the treatment of acne vulgaris for the first time and proved to be effective. This study using oral ciprofloxacin therapy had not been previously published.

Regarding systemic ciprofloxacin plus topical ciprofloxacin solution 74.1% of patients showed good response, 22.5% showed partial improvement and 3.2% had no improvement, while with systemic doxycycline plus topical clindamycin 64.5% of patients showed good response, 29% had partial response and 6.4% showed no response.

Both doxycycline and ciprofloxacin oral therapy in combination with topical clindamycin solution and topical ciprofloxacin solution respectively cleared the lesion in moderate acne within 8 weeks of therapy (64.5% and 74.1% respectively), and when compared the results with each other ciprofloxacin was superior but there was no statistical difference between the two groups ($p > 0.05$).

The combination of oral doxycycline and clindamycin solution showed more effectiveness against pustules rather than papules in all visits ($p=0.0002$) and was statistically significant and was closely comparable to Olafsson et al study [16]. While combination of oral and systemic ciprofloxacin showed no difference in effectiveness against papules and pustules. The side effects of oral ciprofloxacin were well tolerated and considered safe when compared with other systemic therapy like oral isotretinoin. In conclusion, the present study proved the effectiveness of topical plus systemic ciprofloxacin in the treatment of moderate acne vulgaris with negligible side effects.

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