Original Article

Clinical evaluation of roxithromyin in acne vulgaris: comparison of daily versus alternate day regimen

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Abstract Roxithromycin, one of the newer macrolides, has been shown to be effective in acne in some clinical trials. These trials have been done with once or twice daily dosage schedules. As another closely related macrolide, azithromycin, has been shown to be effective when used on alternate days, we conducted this trial to see whether an alternate day regimen of roxithromycin gives comparable results with those of daily regimen or not. One hundred and forty patients were included in the study and were randomly divided in two groups. Patients in Group-I used 300 mg of roxithromycin orally once daily for eight weeks. Those in Group-II used 300 mg of roxithromycin orally on alternate days for eight weeks. Results could be evaluated in 125 patients, with 15 patients lost to follow up. Out of 60 patients in Group-I, 32% showed good(>50%) improvement, 57% moderate (25-50%) and 10% slight (<25%) improvement. Of the 65 evaluable patients in Group-II, 28% showed good, 55% moderate and 14% slight improvement. Using chi-square tests the difference between the results of the two groups was found to be insignificant (p>0.5). Side effects noted were transient and were nausea, slight gastric upset and diarrhea in 10% patients in Group-I and 4.6% patients in Group-II. In conclusion, alternate day dosage regimen is found to be almost equally effective but safer and more economical than daily dosage regimen.

Key words
Roxithromycin, acne vulgaris

Introduction

Acne is a common disease, seen primarily in adolescents and which occurs due to the chronic inflammation of the pilosebaceous units. It is a polymorphic disease in which a variety of lesions are seen such as comedones, papules, pustules, nodules and as a sequelae to active lesions pitted or hypertrophic scars.[1]

Multiple factors are involved in the pathogenesis. These include plugging of the infundibulum of sebaceous ducts, increased production and retention of sebum, overgrowth of *Propionibacterium acnes* and production of inflammation.[2] The anaerobic *P. acnes* proliferates in the obstructed lipid-rich lumen of pilosebaceous units, where O_2 tension is low. It produces biologically active mediators which may lead to

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microcomedo formation as well as induce inflammation.[1,2]

Oral antibiotics are the most widely prescribed oral therapy worldwide. Commonly used antibiotics include tetracycline, oxytetracycline, doxycycline, minocycline, erythromycin and azithromycin.[2] Roxithromycin has been shown to be effective in acne in some clinical trials.[3,4] These trials have been done with once or twice daily dosage schedules. Azithromycin, another closely related macrolide, has been shown to give good results on alternate day regimen.[5,6] We performed this trial to see whether an alternate day regimen of roxithromycin gives comparable results with those of daily regimen or not.

Patients and Methods

It was an open prospective clinical trial. The study was conducted in the out-patient dermatology department of Bahawal-Victoria Hospital, in collaboration with pharmacology department of Quaid-e-Azam Medical College, Bahawalpur. One hundred and forty patients with acne vulgaris were enrolled in the study. The patients with a history of diabetes mellitus, pregnancy, and use of steroids or antibiotics two months earlier were excluded from the study.

Each patient was fully examined and his detailed history was taken. Necessary data including site, size and type of the lesions were recorded on a specified pro forma. The lesions were evaluated and graded according to the following simplified classification suggested by Clark[7]: 1- *mild:* comedones present accompanied by a few superficial inflammatory lesions. 2- *moderate:* Many inflammatory lesions, largely superficial, but more deep-seated pustules evident and tendency of these lesions to scar with time. 3- *severe:* Nodules and cysts with marked scarring.

The patients were randomly divided in two groups. Group-I patients were administered roxithromycin 300 mg/day orally before meals, for 8 weeks. The patients of Group-II were administered roxithromycin 300 mg on alternate days orally, before meals, for 8 weeks. The patients were called after every 2 weeks for follow up. Symptomatic and general improvement was assessed on every visit. Any side effect appeared was noted. Investigations like blood routine examination, renal and hepatic profiles were done at the baseline, after four weeks and at the end of the study.

Overall assessment was done 8 weeks after initiation of therapy. Clinical improvement was graded as follows, 1: good (>50%), 2: moderate (25-50%), 3: slight (<25%), 4: no change, 5: worsening. Adverse effects, when present, were precisely described. Chi-square test was applied for statistical analysis.

Results

At the end of the study, results were evaluated in 125 patients (60 in Group-I, 65 in Group-II). Fifteen patients were lost during follow up. The grades of severity of disease in this study were as follows: 37 % of the patients presented with severe acne, 40% of the patients presented with moderate acne while 23% of the patients presented with mild acne. These patients were almost

Table 1 Patients with various grades of acne.

	Mild	*Moderate*	*Severe*
Group-I (n=60)	15 (25%)	23 (38.3%)	22 (36.7%)
Group-II (n=65)	14 (21.5%)	27 (41.5%)	24 (36.9%)
Total (n=125)	29 (23.2%)	50 (40%)	46 (36.8%)

Table 2 Results of treatment

	Good improvement	*Moderate improvement*	*Slight improvement*	*No improvement*	*Worsening*
Group-I (n=60)	19 (31.7%)	34 (56.7%)	6 (10%)	1 (1.7%)	0
Group-II (n=65)	18 (27.7%)	36 (55.4%)	9 (13.8%)	1 (1.5%)	1 (1.5%)
Total (n=125)	37 (29.6%)	70 (56%)	15 (12%)	2 (1.6%)	1 (0.8%)

evenly distributed in the two groups (**Table 1**). In Group-I, female to male ratio was 4:3, while in Group-II, it was 3:2. Average age of the patients in Group-I was 19±4 years while in Group-I it was 20.5 ± 5 years.

Overall percentage of the patients showing good improvement was 30%; 56% showed moderate improvement whereas 12% showed slight improvement. In Group–I, 32 % of the patients showed good improvement, 57% showed moderate improvement and 10% showed slight improvement. In Group–II, 28% of the patients showed good improvement, 55% showed moderate improvement and 14% showed slight improvement (**Table 2**).

In Group-I, the total percentage of patients showing good or moderate improvement was 88% while it was 83% in Group-II. Statistically the difference in the results of the two groups was not significant (p>0.5). It was also observed that patients suffering from severe and moderate acne showed better response to roxithromycin than patients suffering from mild acne.

With regards to adverse effects nausea, slight gastric upset and diarrhea were noted in 6 (10%) patients of Group-I and 3 (4.6%) patients of Group-II. These side effects were transient and were cured by symptomatic treatment.

Discussion

The present study showed that roxithromycin is an effective drug for acne. The efficacy of roxithromycin in acne is due not only to the reduction in number of *P. acnes*, but also due to inhibitory effects on the production of bacterial lipases, *P. acnes* associated inflammatory mediators and therefore on the activity of neutrophil chemotaxis.[8] Moreover, it is reported that roxithromycin accumulates in the pilosebaceous system and has some anti-androgenic activity.[9,10]

Numerous studies have demonstrated the efficacy and safety of erythromycin in acne, but unfortunately, it is associated with a number of drawbacks including a narrow

spectrum of activity, short half-life, gastrointestinal intolerance and significant number of drug–drug interactions. As the treatment of acne involves long-term therapy with antibiotics, an agent with long tissue half-life can be very useful in increasing the compliance of the patients. The pharmacokinetic profile of the newer macrolides azithromycin and roxithromycin make them suitable agents in this regard.[11]

In the present study, roxithromycin 300 mg daily resulted in good or moderate improvement in 88% of the patients whereas 300 mg of roxithromycin on alternate days showed the same degree of improvement in 83% of the patients. These results are somewhat similar to those of Akamatsu *et al.*[3] who compared 150 mg twice daily with 150 mg once daily of roxithromycin for 8 weeks and found good or moderate improvement in 75% (12/16) and 71.4% (10/14) of the patients in the two groups respectively. However, the ratio of patients (27.7%) showing only good improvement with less frequent dosage schedule (300 mg on alternate days) in our study is much higher than the ratio of the patients (7.1%) showing only good improvement with less frequent dosage schedule (150 mg once daily) observed by Akamatsu *et al.*[3] Kapadia and Talib[5] used azithromycin 500 mg orally thrice weekly for 12 weeks in 35 patients and observed remarkable (60-80%) improvement in 82.9% of the patients. We have seen comparable results with 300 mg of roxithromycin on alternate days.

While treating the patients of acne with antibiotics for long duration it is very important to consider the cost of treatment (especially for poor people of our region), tolerance of the drug and compliance of the patient. The results of the present study indicate that by prescribing 300 mg of roxithromycin on alternate day basis instead of every day, we may reduce the total cost of treatment as well as improve the drug tolerance and patient compliance. However, there is a need for further trials to determine the long-term efficacy and tolerability.

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