Original Article

Comparative study of two different regimens of oral azithromycin in the treatment of acne vulgaris

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Abstract

Background: Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous units. Oral antibiotics are the most widely administered drugs. Azithromycin is one of the antibiotics that has been recently prescribed for acne treatment. There are several protocols of oral azithromycin in the treatment of acne vulgaris.

Objective: The purpose of the present study was to compare two regimens of oral azithromycin in the treatment of acne vulgaris.

Methodology: This randomized open clinical trial was carried out for six (06) months. Total sixty patients with moderate to severe acne were randomly enrolled into two equal groups (group A and B). Group-A received oral azithromycin 250 mg daily for three consecutive days, weekly for 12 weeks. Group-B has been treated with oral azithromycin 500 mg daily on the first day and 250 mg for further two consecutive days weekly for 12 weeks. After the baseline visit patients were assessed 4th week, 8th week, and 12th week. They were assessed for symptom severity, number of comedones, papule, pustule, side effects, and treatment response.

Result: There were no differences between the two groups in decreasing of acne grading score. ($P > 0.05$). The efficacy of a minimal dose was equal to a maximum dose of azithromycin in the treatment of acne. Oral azithromycin in both groups resulted in a significant decrease in acne grading score in each consecutive visit ($P<0.001$).

Conclusion: Azithromycin in low dose 3000 mg monthly as effective as high dose 4000 mg with lower cost, more compliance, and fewer side-effects.

Keyword: Azithromycin, Acne Vulgaris.

Introduction

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous follicles, characterized by seborrhea, comedones, papules, pustules, nodules, and even scars.[1] The comedo is the primary lesion of Acne. The condition usually starts in adolescence and frequently resolves by the mid-twenties.[2] The pathogenesis of acne is multifactorial. It involves excessive sebum production, abnormal epithelial hyperkeratinization in sebaceous follicles, the presence of microbial organisms, notably the anaerobic Propionibacterium acne, and inflammation.[3] Early effective treatment of acne is very important to prevent facial scars that lead to cosmetic and psychological impacts on the patient.

The treatment armamentarium of acne includes topical, oral, and surgical modalities. Topical agents are retinoids, benzoyl peroxide, azelaic acid, salicylic acid, dapsone, erythromycin, clindamycin, and

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surgical modalities.[4] Oral antibiotics like azithromycin, tetracycline, doxycycline, minocycline, lymecycline, erythromycin, amoxicillin, clindamycin, co-trimoxazole, trimethoprim, hormonal therapy, isotretinoin, and occasionally corticosteroids are used for the treatment of acne vulgaris.[5-6] Azithromycin is one of the antibiotics that has been recently prescribed for the treatment of acne which is at least as effective as doxycycline and minocycline.[7-9] It is a nitrogen-containing macrolide antibacterial agent and a methyl derivative of erythromycin with actions and uses similar to those of erythromycin.[10-11] Its extensive distribution in the tissues allows pulse-dose regimen recommendation for increased compliance.[12] Currently some lower dose regimen of azithromycin has been recommended by some authors.[13-14] The current study was conducted to find a low dose regimen of oral azithromycin in the treatment of acne vulgaris which is effective and safe.

Materials and methods:

In this open randomized clinical trial, sixty patients (30 men, 30 women) between the age group of 12 and 45 years and with mild to moderate acne were enrolled from the dermatology outpatient department. Patients with an Investigators Global Assessment (IGA) scale of acne severity score of >2 were considered eligible. Following persons were excluded: i) Patients suffering from nodulocystic acne; ii) Pregnant women and lactating mothers; iii) Women who were taking the oral contraceptive pills; iv) Person having hypersensitivity to azithromycin.

After taking written informed consent selected patients were enrolled into two groups (A and B) by simple randomization method. Group A was treated with azithromycin 250 mg daily for three consecutive days weekly and group B by azithromycin 500 mg on the first day followed by 250 mg daily for two consecutive days weekly. Patients were followed up 4 weekly over 12 weeks and checked for efficacy and adverse effects. At each visit, acne lesions were assessed by a blinded dermatologist to treatment protocols and the IGA scale was used to evaluate the response of patients to treatment. The efficacy of each protocol was investigated by comparing the decrease of acne score at each visit, with the baseline and previous session grade. The efficacy and adverse effects of the two modalities were compared. Computer-based statistical analyses were carried out with appropriate techniques and systems. All data were recorded systematically in preformed data collection form (questionnaire) and quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. Statistical analysis was performed by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-17) (SPSS Inc, Chicago, IL, USA). 95% confidence limit was taken. Probability value <0.05 was considered as the level of significance. The association between qualitative variables was measured by the Chi-Square test. The student's t-test has been performed to see the association between quantitative variables. Before the commencement of this study, the research protocol was approved by the ethical committee (Local Ethical committee) of the Shahid Mansur Ali medical college and hospital, Dhaka.

Results:

Equal thirty patients in both groups have completed the treatment and the follow-up period. There are no differences between the two groups in decreasing of acne grading score (p >0.05). However, the mean acne score had significantly decreased at the end of the first, second, the third months after treatment when compared to baseline. P<0.001 (table-I).

Table I: Total Acne score in different follow-up

Total Acne score	Groups		p value*
	Group A (n=30)	Group B (n=30)	
Baseline	33.60 ± 5.98	33.53 ± 5.68	0.965
1st follow up	22.20 ± 4.73	24.03 ± 4.66	0.135
2nd follow up	8.27 ± 2.02	14.23 ± 3.15	0.001
3rd follow up	2.27 ± 1.08	6.27 ± 1.57	0.001
Percent of reduc on from baseline to 3rd follow up	93.24 ± 3.11	81.17 ± 4.22	0.001

*t-test was done to measure the level of significance.

Data were shown as Mean ± SD.

At baseline mean of total acne score was 33.60 ± 5.98 and 33.53 ± 5.68 in group A and B (p=0.965), at 1st follow up it was 22.20 ± 4.73 and 24.03 ± 4.66 respectively in group A and B (0.135), at 2nd follow up it was 8.27 ± 2.02 and 14.23 ± 3.15 (p=0.001) and at final follow up it was 2.27 ± 1.08 and 6.27 ± 1.57 respectively in group A and B (p=0.001). Percent reduction of acne severity from baseline to final follow up was 93.24 ± 3.11 in group A and 81.17 ±

4.22 in group B (p=0.001)

Discussion:

Azithromycin has significant anti-inflammatory and immunomodulatory properties by suppressing different cytokines and substances including IL-1 α,IL-8, PGE2, reactive oxygen species (ROS), and nitric oxide (NOx). It also works by inhibiting the chemotaxis of neutrophils.[15] At first, Fernandes-Obregon recommended azithromycin for the treatment of acne vulgaris.[7] There is no doubt that azithromycin is an effective antibiotic in the treatment of acne vulgaris.[8-9,11,13] Different regimens of azithromycin are recommended and practiced for the treatment of acne by different authors and practitioners for the treatment of acne.[13,16-20] Kapadia et al recommended 500 mg thrice weekly for 12 weeks.[20] Bardazzi et al conducted a study with the same regime and found it effective and convenient.[17] The regimen consisting of azithromycin 500 mg daily for three consecutive days in every 10 days for 12 weeks is mostly practiced pulse therapy in acne.[18,21-22] Prasad et al treated acne with 500 mg daily for 4 days a month for three months.[23] The study was carried out to compare the efficacy and safety of azithromycin 250 mg daily three consecutive days weekly and azithromycin 500 mg on the first day and 250 mg daily for further two consecutive days in the treatment of acne vulgaris with follow up at week 4, 8 and 12. Mean scores for open comedones, closed comedones, papule, and pustule were identical between the two groups at baseline (P>0.05). Significantly better reduction of acne score for open comedones, closed comedones, papule, pustule, and total acne score was noticed at 2nd and 3rd follow up (p<0.005) in group A than the group B. Percent reduction of acne severity from baseline to final follow up was 93.24 ± 3.11 in group A (azithromycin 250 mg daily for three consecutive days, weekly) and 81.17 ± 4.22 in group B (azithromycin 500 mg on the first day then 250 mg daily further two consecutive days, weekly) (p=0.001) (Table I).

Fernandez-Obregon found azithromycin 250 mg thrice weekly safe and effective in the treatment of acne.[8] Naineni and Akrami recommended a lower dose (1500 mg monthly total) as convenient, safe, effective, and cheap.[19] In a similar type of study Innocenzi et al, conducted an open-label, noncomparative study for 12 weeks.[13] In another randomized clinical trial, Basta-Juzbasic et al showed that azithromycin in a total dose of 6.0 g in 10 weeks is an excellent and effective regimen for papulopustular acne with few side effects and good patient compliance.[24]

In the study by Kapadia and Talib maximum clearance (80%) was observed at 12 weeks.[20] Fernandez-Obregon found significant improvement after 4 weeks.[8]

In this study, azithromycin 250 mg daily for three consecutive days of a week (3000 mg per month) had a better response than azithromycin 500 mg on the first day and 250 mg for further two consecutive days of the week (4000 mg per month). Overall tolerability of azithromycin with the commonly used regimens is good and patients can experience few minor adverse effects few gastrointestinal complaints including nausea, abdominal pain, and diarrhea.[17-19] In the current study no such adverse event was experienced.

Conclusion:

Low-dose azithromycin comprising 3000 mg per month is an effective and cost-effective regimen for the management of acne vulgaris.

Conflict of interest:

No.

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