

## ORIGINAL ARTICLE

## COMPARISON OF ORAL AZITHROMYCIN WITH ORAL DOXYCYCLINE IN THE TREATMENT OF ACNE VULGARIS

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**Background:** Acne vulgaris is a common inflammatory disorder of the skin that involves pilosebaceous units. This study was conducted to compare the efficacy of oral azithromycin with oral doxycycline in the treatment of acne vulgaris in our population. **Methods:** This randomized controlled trial was conducted in the dermatology department of Lady Reading Hospital, Peshawar from January to December 2011. All male and female patients of age (14–30 years) having moderate acne vulgaris on face only were included in the study. Patients were randomly divided into two groups. Patients in first group were given azithromycin 500 mg daily before meal for 4 consecutive days monthly for 3 months while patients in second group were given doxycycline 100 mg daily after meals for 3 months. Patients were followed up after taking treatment for three months to see the response of each drug. Response was graded as excellent, good, moderate, mild and no response. **Results:** A total of 386 patients equally divided in azithromycin and doxycycline groups. Male to female ratio in azithromycin and doxycycline groups was 0.82:1.11 and 0.89:1.04 respectively. Mean age in both groups was  $18.45 \pm 2.91$  years and  $17.96 \pm 2.59$  years respectively. In azithromycin group, an excellent response was noted in 6 (3.1%), and good response was observed in 44 (22.8%) patients. In doxycycline group 22 (11.4%) patients had excellent and 107 (55.4%) patients had good response. The difference being statistically significant. **Conclusion:** Doxycycline is a better option for treatment of acne vulgaris as compared to azithromycin.

**Keywords:** Doxycycline, Azithromycin, Acne vulgaris

J Ayub Med Coll Abbottabad 2014;26(1):64–7

## INTRODUCTION

Acne vulgaris is a common inflammatory disorder of the skin that involves pilosebaceous units.<sup>1</sup> Pathogenesis of acne is multifactorial and is thought to involve excess sebum production, follicular hyperkeratinization, bacterial colonization, and inflammation.<sup>2</sup> Key factor in pathogenesis is genetic.<sup>1</sup> If both parents have acne, 3 out of 4 children will have acne, if one parent has acne, then 1 out of 4 children will have acne. Similar to other genetic conditions, acne sometime skips generations.<sup>3</sup>

Many therapeutic options exist for treating acne including topical benzoyl peroxide, topical and oral antibiotics, topical and oral retinoids and oral contraceptives.<sup>2</sup> During the last 2–3 decades, systemic antibiotics, mainly tetracyclines and macrolides, have assumed main role in the management of acne patients with inflammatory papules, pustules and cysts. They require frequent administration and are sometimes associated with side effects, contributing to reduced compliance.<sup>4</sup>

Azithromycin is a macrolide that has been recently prescribed for the treatment of acne. It is as effective as doxycycline and minocycline.<sup>5</sup> Azithromycin is a nitrogen containing macrolide antibacterial agent and a methyl derivative of erythromycin with action and uses similar to those of

erythromycin.<sup>6,7</sup> Its extensive distribution in the tissue allow pulse-dose regimen recommendation for increased compliance.<sup>8</sup> Due to its improved pharmacokinetic properties, high tolerability profile and efficacy against *Propionibacterium acnes*,<sup>6</sup> the rationale for the use of azithromycin in acne has been examined and it has been found to be effective in a few clinical studies.<sup>5,9</sup>

Tetracyclines are the first-line anti-acne antibiotics. However tetracyclines may be associated with a fairly large number of adverse effects and comparative clinical trials have shown that azithromycin's tolerability profile is superior to conventional anti-acne treatment such as erythromycin, and doxycycline.<sup>1</sup> Another comparative study showed that there was 77.26% improvement in azithromycin treated group in comparison to 63.74% in doxycycline treated group.<sup>4</sup>

On the basis of previous studies azithromycin was thought to have superior therapeutic effect to doxycycline, but we hypothesized that doxycycline is better than azithromycin and if accepted than it will be recommended for local physicians due to low cost and high efficacy. Since no local study has been done to compare the efficacy of doxycycline and azithromycin, therefore it seems worthwhile to

conduct this study so that patients are managed effectively and efficiently. The objective of this study was to compare the efficacy of oral azithromycin with oral doxycycline in treatment of acne vulgaris in our population.

**MATERIAL AND METHODS**

This prospective randomized controlled trial was conducted in dermatology department Lady Reading Hospital Peshawar over a period of one year from January 2011 to December 2011. Sample size was 193 in each group, using 77.26%<sup>4</sup> improvement in azithromycin, 63.74%<sup>4</sup> improvement in doxycycline, 5% level of significance and 90% power, using the WHO software for sample size determination in health studies. Formula for hypothesis test for two proportions (one-sided) was used with the aforementioned assumptions. Randomization was done using lottery method. Both male and female patients of acne vulgaris between ages of 14–30 years with moderate acne vulgaris (on face only) were included and all pregnant, breast feeding, Acne (fulminans, conglobata), history of use of Isotretinoin therapy within past 6 months, topical treatment in last 2 weeks, use of other systemic antibiotics in the month prior to study were excluded from the study.

After taking permission from the hospital Ethical Committee all patients coming to dermatology OPD and fulfilling inclusion criteria were enrolled for the study. Written informed consent was taken from enrolled patients. Detailed history was taken and complete physical examination was performed to rule out associated diseases. Patients were divided into two groups using lottery method. Patients in first group were given azithromycin 500 mg daily before meal for 4 consecutive days each month for 3 months. Patients in second group were given doxycycline 100 mg daily after meals for 3 months. Patients were followed up after three months to determine response of each drug. Efficacy assessed in terms of disappearance of characteristic lesions of acne vulgaris (white heads, black heads, red spots and red bumps) and was measured by disappearance of lesions in terms of percentages as: Excellent (100%), Good (80–90%), Moderate (50–79%), Mild (30–49%), and No Response (<than 30%).

Data was collected on a *pro forma* and analysed using SPSS-16. Chi-square test was used to check the efficacy by comparing the excellent, good, moderate, mild and no response of both the drugs and *p*-value ≤0.05 was considered as significant.

**RESULTS**

A total of 386 patients were included in the study and were divided into group-1, who were given Azithromycin and group-2, which were given

Doxycycline. Each group was having 193 patients and no patient was lost from the study. Total number of male and female patients was 171 and 215 respectively. The age of the patients ranged from 14–30 years. Maximum numbers of patients were in the 2<sup>nd</sup> decade of their lives. In group-1, there were 82 (42.5%) males while in group-2 male patients were 89 (46.1%). Mean age in group-1 was 18.45±2.91 years, while in group-2, it was 17.96±2.59 years. Most of the patients in both groups were in age range of 14–22 years shown in Table-1.

In Azithromycin group, an excellent response was noted in 6 (3.1%), good response in 44 (22.8%), moderate response in 115 (59.6%), mild response in 22 (11.4%) and no response was observed in 6 (3.1%) patients. In Doxycycline group excellent response was noted in 22 (11.4%), good response in 107 (55.4%), moderate response in 51 (26.4%), mild response in 12 (6.2%) and no response was observed in 1 (0.5%) patients as shown in table-4. The response as a whole in all grades was statistically significant with *p*-value less than 0.05.

**Table-1: Patients by Age in both groups**

Age	Groups		Total n (%)
	Azithromycin n (%)	Doxycycline n (%)	
≤ 18	114 (59.1)	118 (61.1)	232 (60.1)
19–22	65 (33.7)	69 (35.8)	134 (34.7)
23–26	10 (5.2)	5 (2.6)	15 (3.9)
27+	4 (2.1)	1 (0.5)	5 (1.3)
<b>Total</b>	<b>193 (100.0)</b>	<b>193 (100.0)</b>	<b>386 (100.0)</b>

**Table-2: Response to treatment by groups**

Response	Groups		Total n (%)
	Azithromycin n (%)	Doxycycline n (%)	
<b>Excellent</b>	6 (3.1)	22 (11.4)	28 (7.3)
<b>Good</b>	44 (22.8)	107 (55.4)	151 (39.1)
<b>Moderate</b>	115 (59.6)	51 (26.4)	166 (43.0)
<b>Mild</b>	22 (11.4)	12 (6.2)	34 (8.8)
<b>No Response</b>	6 (3.1)	1 (0.5)	7 (1.8)
<b>Total</b>	<b>193 (100.0)</b>	<b>193 (100.0)</b>	<b>386 (100.0)</b>

*p*-value: 0.000

**DISCUSSION**

Acne vulgaris is a chronic inflammatory skin disorder that involves pilosebaceous units. No individual passes through adolescence without few comedones and papules.<sup>4,10</sup> Effective treatment is essential to prevent facial scars that leads to cosmetic and psychological impact to the patient.<sup>11</sup> Oral antibiotics known to be effective in the treatment of acne are oxytetracycline, macrolides, minocycline, doxycycline, and trimethoprim.<sup>12</sup> Clinical isolates of *Propionibacterium acnes* are known to be highly susceptible to azithromycin.<sup>13</sup> *Propionibacterium* resistance to antibiotics is an emerging problem.

Patients with previous antibiotic use may be less likely to respond to their current treatment. It has also been shown that resistant strains of *Propionibacterium acnes* are also associated with treatment failure.<sup>14</sup> There is no data on acquiring resistance of *Propionibacterium acnes* to azithromycin, however, azithromycin resistance in *Streptococcus pyogenes*, a pathogen which causes a wide spectrum of community-acquired infections varies between 20% and 27.4%.<sup>15,16</sup>

A study Naieni FF *et al*<sup>17</sup> compared three regimens of oral azithromycin in the treatment of acne. First group received azithromycin on five consecutive days, 500 mg on the first day and 250 mg daily for a further four days per month. Second group received 500 mg daily for four consecutive days per month and last group received 250 mg thrice weekly. Patients assessed after 12 weeks, found no difference between three groups in the treatment of acne. In our study we compared regimen of 500 mg daily for four consecutive days per month with 100 mg daily doxycycline. The result of azithromycin was comparable with this study, because of similarity in age group, type of acne and given treatment regimen.

Prasad D *et al*<sup>11</sup> compared azithromycin 500 mg for 4 days per month with 100 mg doxycycline per day. They found that doxycycline 100 mg daily to be as effective as azithromycin 500 mg for 4 days in a month. But results of our study showed that 100mg daily doxycycline was better than same dosage regimen of azithromycin. The reason of disparity between our study and the referred study could be their small sample size (total 60 patients), concomitant application of 0.05% tretinoin cream in both groups, and inclusion of patients of moderate to severe acne vulgaris.

In our study doxycycline was better option for acne vulgaris as compared to azithromycin, but study done by Singhi MK,<sup>4</sup> who compared azithromycin 500 mg daily for three consecutive days in a 10 days cycle with daily 100 mg doxycycline. He found that azithromycin was better than doxycycline in the treatment of acne. He enrolled 70 patients in his study. He also prescribed topical erythromycin to both groups. He included those patients in his study that had moderate to severe acne. In our study we enrolled 386 patients having moderate acne only on face and with no use of topical medication. Therefore our study results are different from the referred study.

Fernandez *et al*<sup>5</sup> prescribed for the treatment of his enrolled patients azithromycin 250 mg per day for 3 days in a week. After 4 weeks he found 85% reduction in acne lesions compared with 77.1% for other antibiotics (doxycycline, tetracycline and minocycline). His study showed that azithromycin was better than doxycycline. Because of only four

weeks of therapy in his study, our study showed better result for doxycycline as compared to azithromycin due to continuation of therapy for 12 weeks.

Gruber *et al* compared minocycline and azithromycin. In this study azithromycin was used in 3 cycles each month. He repeated the cycle after every 10 days and gave azithromycin for 4 days in a dose of 500 mg/day in each cycle. Azithromycin was found to be at least as effective as minocycline.<sup>9</sup> The disparity of our study results from referred study could be due to different regimen of azithromycin.

Our findings suggested that doxycycline was significantly better than azithromycin in the treatment of moderate acne vulgaris. More than 80% improvement was seen in 107 (55.4%) patients in doxycycline group, but only 44 (22.8%) in the azithromycin group. Overall there was more improvement in doxycycline group in comparison to azithromycin group and this difference was statistically significant.

The limitation of this study was different dosage of azithromycin, concomitant with topical medication and multiple randomized controlled trial are needed to determine optimal dose, duration and compliance issues to generate local data.

## CONCLUSION

The conclusion of this study is that in the age range of 14–30 years daily oral doxycycline is better than azithromycin in the treatment of moderate acne vulgaris.

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