Comparison of oral azithromycin pulse with daily doxycycline in the treatment of acne vulgaris

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ABSTRACT

Introduction: Oral azithromycin has been advocated by some in the treatment of acne. However, its efficacy has not been established. **Material and Methods:** This non-randomized controlled trial was conducted on 70 outpatients with acne vulgaris to compare the efficacy and safety of azithromycin and doxycycline in the treatment of inflammatory acne. In the first group, azithromycin was administered 500 mg daily before meals for 3 consecutive days in a 10-day cycle, with the remaining seven days in each cycle being drug-free days. The second group was given doxycycline 100 mg daily after meals. Topical erythromycin was prescribed to all patients. Clinical assessment was done at 10-day intervals for both the groups up to three months. We followed the severity index described by Michaelsson for assessment of outcome measures. **Results:** There was 77.26% improvement in azithromycin treated group in comparison to 63.74% in the doxycycline treated group. There was a statistically significant reduction in severity in the azithromycin treated group. **Conclusion:** The study showed that a combination of azithromycin with topical erythromycin was significantly better than doxycycline with topical erythromycin in the treatment of acne vulgaris. The incidence and severity of side effects were also lower with azithromycin.

Key Words: Azithromycin, Acne Vulgaris, Doxycycline

INTRODUCTION

Acne vulgaris is the most common dermatological disorder in adolescence. As a matter of fact, no individual transits through adolescence without a few comedones and papules.[1] For the last 2-3 decades, systemic antibiotics, mainly tetracyclines and erythromycins, have assumed the main role in the management of acne patients with inflammatory papules and cysts. They require frequent administration and are sometimes associated with side effects, contributing to reduced compliance.[2] Hence, we studied the efficacy and safety of oral azithromycin and topical erythromycin in the treatment of acne vulgaris in comparison to oral doxycycline and topical erythromycin.

Azithromycin belongs to the azalide group of antibiotics and is closely related structurally to macrolides like erythromycin. It is more tissue stable, penetrates deeply into tissue and has a higher terminal half-life than erythromycin. It is approved mainly for the treatment of streptococcal pharyngitis and uncomplicated skin infections.

MATERIAL AND METHODS

Seventy patients participated in the study, of whom 62 completed it. All of them had moderate to severe acne as proposed by a Consensus Conference for the Classification of Acne,[3] and had not responded to conventional therapy. Patients taking antibiotics for any other reason, pregnant women and patients of

liver disease were excluded. Fifty five patients had lesions over the back and chest too. Most of the patients had acne since two years and a few, since 5 years.

In all the cases the acne lesions were graded according to the severity index described by Michaelsson et al[4] by counting the number of open or closed comedones, papules, pustules, and infiltrated and cystic lesions. Michaelsson described the severity index as 0.5 for comedones, 1 for papule, 2 for pustules, 3 for infiltrated lesions and 4 for cystic lesions. The total severity score of disease was calculated by multiplying each type of lesion with its severity index and adding them together.

Patients were divided into two groups. The first group was given azithromycin 500 mg daily before meals for 3 consecutive days in a 10-day cycle, with the remaining seven days in each cycle being drug-free. The second group was given doxycycline 100 mg daily after meals. Topical erythromycin twice daily was prescribed to all patients. Patients were clinically assessed at 10-day intervals for up to three months. Each time the severity index of the disease was calculated and recorded by two clinicians (the average of the two scores was taken), and clinical photographs were taken. The final clinical assessment was done and the severity index was calculated at the end of the third month.

RESULTS

Seventy patients participated in the study, 45 female and 25 male; 32 were treated with doxycycline and 38 with azithromycin (Table 1). Six patients (4 from the doxycycline and 2 from the azithromycin group) were lost to follow up. In two doxycycline treated patients, treatment was withdrawn due to serious side effects: one had esophageal ulceration and another had photo-onycholysis. Sixty two patients completed the study. The mean severity index for the azithromycin group declined from 254.96 pretreatment (range 153.5 to 446.5) to 59.93 after treatment for 90 days (range 15-266), an improvement of 77.26% on average (Table 2). In 19 (52.8%) patients there was > 80% improvement, in 13 patients (36.1%) there was 40-80% improvement, and only 4 (11.1%) had less than 40% improvement. There was an average of 10% improvement after the first cycle, about 50% after 4 cycles, and 72% after 8 cycles. Three patients complained of slight gastric upset but the drug did not need to be discontinued.

In the doxycycline treated group, the mean severity index declined from 234.76 (range 178-365.5) at the start of the study to 82.85 (range 32-234) after treatment for 3 months, an overall improvement of 63.74%. More than 80% improvement was seen in 5 (19.23%) patients, 40-80% in 16 (61.54%) and less than 80% improvement in 5 (19.23%) patients. There was only 12% overall improvement, which was nearly 50% after 60 days improvement. Three patients had diarrhea, four gastric upset, one esophageal ulceration and one, photo-onycholysis.

The severity reduction was compared with both drugs and it was tested with t-test for difference between the means; this also showed significant change in the reduction of lesions. The mean severity index of the two drugs was 254.94 ± 70.39 for azithromycin and 234.76 ± 54.71 for doxycycline. After treatment the mean score reduced to 55.93 ± 55.68 and 82.85 ± 59.4 respectively.

There was a significant difference between the severity reduction when comparing the effects of azithromycin and doxycycline ($p < 0.01$). Similarly when proportions were compared with the two drugs, viz. azithromycin and doxycycline, this showed a significant reduction after 3 months and the percentage decrease was around

Table 1: Comparison of percentage severity reduction of azithromycin and doxycycline

Severity reduction (%)	Azithromycin	Doxycycline	Total
Less than 40%	4 (11.0%)	5 (19.23%)	9 (19.23%)
41-80%	13 (36.1%)	16 (61.54%)	29 (41.94%)
> 80%	19 (52.8%)	5 (19.23%)	24 (38.71%)
Total	**36**	**26**	**62**

p < 0.01

Table 2: Mean severity index of both the groups before and after treatment

Patients	Mean severity index		Decrease percentage
	Initial	After 3 months	
Azithromycin (36)	254.96 (153.5 - 446.55)	59.93 (15 - 266)	77.26
Doxycycline (26)	234.76 (178 - 365.5)	82.85 (32 - 234)	63.74

p < 0.05

77.26% and $p < 0.05$.

DISCUSSION

Our findings suggested that a combination of azithromycin and topical erythromycin was significantly better than doxycycline and topical erythromycin in the treatment of inflammatory acne vulgaris. More than 80% improvement was seen in 19 (52.8%) patients in the azithromycin group, but only 5 (19.2%) in the doxycycline group. Overall there was 77.26% improvement in the azithromycin group in comparison to 63.74% in the doxycycline group and this difference was statistically significant.

Similar results were obtained by Fernandez et al[5] who gave 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). Prasad D et al[6] found doxycycline 100 mg daily to be as effective as azithromycin 500 mg for 4 days in a month. As the effect of the azithromycin lasts for 10 days, we tried the 10-day cycle in our treatment regimen. Plewig et al[7] found that 33% of patients had good to excellent response (50-75%) to doxycycline in acne vulgaris, which is comparable to our results (38.71% had more then 80% reduction). Gruber et al[8] compared azithromycin with minocycline and observed a satisfactory clinical response (70-75%) with both the drugs. These findings suggest that azithromycin is a better alternative in patients with moderate to severe acne and has no serious side effects.

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