Efficacy of Oral Azithromycin versus Doxycycline in the Treatment of Acne Vulgaris

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ABSTRACT

Introduction: Acne vulgaris is one of the most common skin disease affecting adolescence of either sex, globally. Antibiotics like macrolides and tetracycline have been used with good results, studies comparing their efficacy are lacking. The present study compare the efficacy of Azithromycin v/s Doxycycline in acne vulgaris. **Aims:** To compare the efficacy of Azithromycin and Doxycycline in the treatment of acne vulgaris. **Methods:** This is a prospective hospital based comparative study, conducted on 80 patients attending outpatient department of Dermatology, Nepalgunj Medical College Teaching Hospital with acne vulgaris from July 2019 to April 2020. Patient were divided alternately into two groups, Group A received Azithromycin (n=40) and Group B Doxycycline (n=40) and compared the effects of treatment at 6 and 12 weeks. Efficacy assessment was done according to simple acne grading system. **Results:** Acne was predominant in female (62.5%) as compared to male (37.5%). Patient between 16 to 20 years age group were more prone to acne (47.5%). Most of the patients had Grade II acne before treatment in both groups (Azithromycin 52.5%, Doxycycline 55%). After the treatment most of them improve to Grade I at 6 weeks (Azithromycin 50%, Doxycycline 55%) and to Grade zero at 12 weeks (Azithromycin 42.5%, Doxycycline 67.5%).There was no statistically significant difference in treatment efficacy between the two groups at 6 weeks but at 12 weeks efficacy of Doxycycline was significantly better than Azithromycin. **Conclusion:** Both oral Azithromycin and Doxycycline when given for treatment of acne vulgaris the analysis showed good improvement after 6 weeks of treatment but there was no statistically significant difference in the improvement in both groups (p 0.771). However after 12 weeks patient receiving Doxycycline showed statistically significant improvement (p 0.035) in comparison to the patients receiving Azithromycin.

Keywords: Acne vulgaris, Azithromycin, Doxycycline, Efficacy

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INTRODUCTION

Acne vulgaris is one of the most common chronic inflammatory disease with a prevalence rate of 9.4% globally, making it the eighth most prevalent disease throughout the globe[1] The condition usually initiates around the age of 12 to 14 years and their prevalence decreases after 18 years.[2,3] However, population and sex-based epidemiological studies show that it persists (7 to 17%) beyond the age of 25 years[4] and tend to effect women at higher rate than male.[5] Clinical manifestation is characterized by comedones, papules, pustules, nodules, cysts and scars.[6] The pathogenesis is multifactorial, which includes androgen-mediated stimulation of sebaceous gland activity, abnormal keratinization leading to follicular plugging, inflammation of the follicle, and surrounding dermis due to Propionibacterium acnes.[7] Besides above-mentioned conditions this disease tends to affect and has a direct correlation with patients self-image, impacting considerably on their emotional, physical appearance, health and quality of life.[8] Many therapeutic options exist for treating acne including topical and oral antibiotics.[9] For the last 2 to 3 decades, systemic antibiotics, mainly tetracycline and macrolides, have been used as first-line treatment in the management of acne patients.[10] The efficacy of these agents depends on their ability to reach the lipid-rich environment of the pilosebaceous follicles and inhibition of protein synthesis of P. acnes, thus exerting bacteriostatic, and sometimes bactericidal effects. Thus, the choice of systemic antibiotic agents for treating acne include Azithromycin and Doxycycline in clinical practice worldwide.[11] Further more severe adverse effects of systemic antibiotics in person treated for acne are uncommon.[12]

METHODS

This prospective comparative study was conducted from July 2019 to April 2020 on 80 patient who presented with acne vulgaris in outpatient department of Dermatology, Nepalgunj Medical College Teaching Hospital, Banke, Nepal. Ethical clearance was obtained from institutional review committee (IRC) NGMC. Thus this study was undertaken to compare the efficacy of Azithromycin and Doxycycline respectively in the treatment of acne vulgaris.

Patients with acne vulgaris of grade II, III, and IV, between 13 to 35 years of both gender and who gave consent to participate in the study were included. Pregnant, lactating mothers and patient under medications like isotretinoin, oral contraceptives etc. which could possibly interfere with the course of disease were excluded. After selecting alternatively 80 acne vulgaris patients meeting our criteria were taken in 12 weeks therapy plan. Patients were divided into two groups: Group A (n=40) were scheduled to receive oral Azithromycin 500mg once daily three times a week, and Group B (n=40) who received oral Doxycycline 100mg once daily. Topical Adapalene 0.1% was given to all the patients.

Severity of acne was assessed using Simple Acne Grading System.[13]

Grade I: Comedones, occasional papules.
Grade II: Papules, comedons, few pustules.
Grade III: Predominent pustules, nodules, abscesses.
Grade IV: Mainly cysts, abscesses, widespread scaring.

Post treatment follow up: Patients were followed up after 6 weeks and 12 weeks. If the patient after treatment went into lower grades from the higher grades as for example Grade IV to III, Grade III to II, Grade II to I and some patients to Grade zero (The patient were placed in Grade zero if there was nonexistence of the lesion at the end of treatment) it was considered as a criteria of improvement.

Statistical Analysis

Data was analysed using SPSS20. Chi square test, Fisher's exact test and Wilcoxin signed ranks test were used. 'p' value less than 0.05 was considered significant.

RESULTS

In our study, out of 80 patients, 30 (37.5%) were males and 50 (62.5%) were females. The data demonstrates female predominance in symptoms ratio as compared to male patients. This study further showed that the prevalence of acne was highest among the age group 16 to 20 (47.5%), as compared to other age groups namely, 10 to 15 (18.75%), 21 to 25 (18.75%), 26 to 30 (12.5%) and 31 to 35 (2.5%) respectively.

The mean age of acne vulguris was 20.1±4.74 for Azithromycin and 19.35±4.89 for Doxycycline respectively. There was no significant difference in age (p value 0.489).

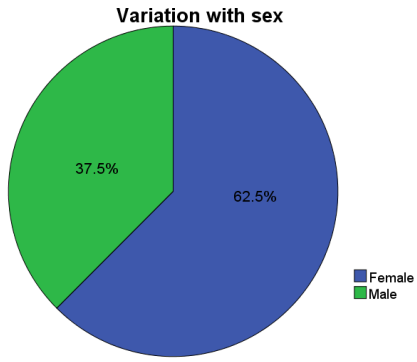

Figure 1: Comparison of gender between the groups.

Gender distribution in female was higher in both the groups

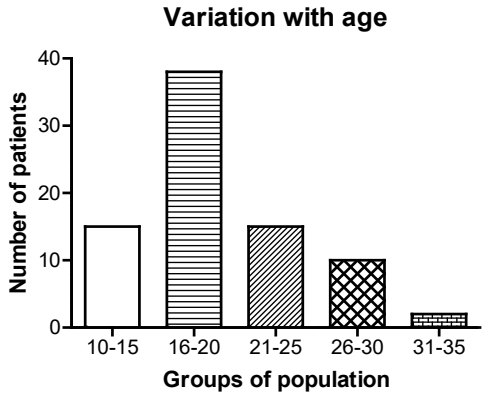

Figure 2: Variation with age.

Most of the patients were between 16-20 years of age.

Treatment Group	Pre-treatment Grade of Acne			Total	Exact Sig. (2 sided)
	Grade II	Grade III	Grade IV		
Group A	21 52.5%	12 30%	7 17.5%	40 100%	
Group B	22 55%	7 17.5%	11 27.5%	40 100%	0.328
Total	**43 53.8%**	**19 23.8%**	**18 22.5%**	**80 100%**	

Table I: Comparisons of pre-treatment grade of acne between the groups.

There was no any statistically significant difference in pre-treatment grade of acne between the two groups.

Treatment Group	Treatment at 6 weeks						Exact Sig. (2 sided)
	Grade zero	Grade I	Grade II	Grade III	Grade IV	Total	
Group A	0 0%	20 50%	15 37.5%	5 12.5%	0 0%	40 100%	
Group B	0 0%	22 55%	12 30%	6 15%	0 0%	40 100%	0.771
Total	**0 0%**	**42 52.5%**	**27 33.8%**	**11 13.8%**	**0 0%**	**80 100%**	

Table II: 6 weeks follow up analysis of the treatment efficacy between the groups.

At 6 weeks there was no any statistically significant difference in grade of acne between the two groups.

Treatment Group	Treatment at 12 weeks						Exact Sig. (2 sided)
	Grade zero	Grade I	Grade II	Grade III	Grade IV	Total	
Group A	17 42.5%	17 42.5%	6 15%	0 0%	0 0%	40 100%	0.035
Group B	27 67.5%	12 30%	1 2.5%	0 0%	0 0%	40 100%	
Total	**44 55%**	**29 36.2%**	**7 8.8%**	**0 0%**	**0 0%**	**80 100%**	

Table III: 12 weeks follow up analysis of the treatment efficacy between the groups.

At 12 weeks Doxycycline group showed statistically significant improvement in grade of acne in comparison to Azithromycin group.

Treatment Group	Side Effects						
	None	Nausea	Abdominal pain	Diarrhoea	Headache	Photo-sensitivity	Total
Group A	34 85%	2 5%	3 7.5%	1 2.5%	0 0%	0 0%	40 100%
Group B	31 77.5%	5 12.5%	1 2.5%	0 0%	2 5%	1 2.5%	40 100%
Total	**65 81.2%**	**7 8.8%**	**4 5%**	**1 1.2%**	**2 2.5%**	**1 1.2%**	**80 100%**

Table IV: Comparison of side effects between the two groups.

The result shows that most of the patient had Grade II acne before treatment in both groups (Azithromycin 52.5%, Doxycycline 55%).After the treatment at 6 weeks Group A patients receiving Azithromycin 50% were in Grade I, 37.5% in Grade II, 12.5% in Grade III where as in Group B patients receiving Doxycycline 55% were in Grade I, 30% in Grade II and 15% in Grade III. Although the treatment with Doxycycline showed a marginal difference in the improvement rate it was statistically not significant (p 0.771). After the treatment at 12 weeks Group A patients receiving Azithromycin 42.5% were in Grade zero, 42.5% in Grade I, 15% in Grade II where as in Group B patients receiving Doxycycline 67.5% were in Grade zero, 30% in Grade I and 2.5% in Grade II. The treatment with Doxycycline showed overall improvement which was statistically significant (p 0.035).

DISCUSSION

Acne vulgaris is the most common chronic inflammatory skin disease affecting in late adolescence throughout the globe and affecting the population of both the sex, the medication for the treatment of choice is still lacking.[6,14] Systemic antibiotics have been the mainstay of treatment for moderate to severe acne vulgaris to date. The effectiveness of several antibiotics, including oxytetracycline, minocycline, doxycycline, erythromycin and azithromycin, in treating acne has been established.[6,8] Clinical efficacy is often noticed within 6 to 8 weeks of antibiotics inititation but can be given for 12 to 18 weeks or even more.[15] In this study we tried to compare the efficacy of oral azithromycin with doxycycline in treatment of acne vulgaris. A study by Adityan et al has shown that acne has female preponderance in comparison to male and the average age of patient presenting with acne vulgaris in outpatient department was 19.78± 4.94.[13] Similar to the study done by Aditya et al the present study shows female preponderance, female: male ratio = 62.5% : 37.5%. Further other studies also have shown that age around 15 to 18 has been the dominant phase of acne development.[14] The result of our study shows 16 to 20 years age group are more prone to acne vulgaris. These results validate that the development of the disease and the effecting group is almost similar throughout the globe. In our study there was significant improvement in treatment outcome at both 6 and 12 weeks in both azithromycin and doxycycline groups. This study is in consistent with study done by Kus S, Yucelten D, Aytug A, where both azithromycin and doxycycline given for treatment of acne vulgaris showed significant improvement for the facial lesion.[16] Similarly, study done by Amatya A et al showed both azithromycin and doxycycline are effective in treatment of acne.[11] Study done by Kumar S et al. also shows that both azithromycin and doxycycline have good outcome in acne vulgaris.[6] There is no any statistically significant difference between their response when compared with each other at 6 weeks but there was significantly better outcome in Doxycycline group at 12 weeks follow-up (p=0.771, p=0.035 respectively). A study done by Maleszka et al[17] showed that there was consistently higher reduction in acne lesions with doxycycline than azithromycin treatment. A study done by Kus S, Yucelten D, Aytug A, showed that the efficacy of Azithromycin and Doxycycline given for treatment of acne vulgaris had no significant difference between the treatment outcome.[16] In contrast to our study, a study done by Gruber F et al[18] showed that azithromycin is more effective in the treatment of acne, when compared with doxycycline. Similarly, the study conducted by Singhi MK et al. found that there was a significant difference between the severity reduction with azithromycin when comparing the effects of azithromycin and doxycycline ($p < 0.01$).[10]

The present study shows better outcome in 12 weeks treatment when compared with 6 weeks treatment with either drugs. A study done by Innocenzi et al. also suggested that for best therapeutic result systemic antibiotics should be continued till 12 weeks.[8] Patients in Doxycycline group experienced more side effects 22.5% compared to patients in group Azithromycin 15%. Similar to our study a study done by Amatya A et al patients in Doxycycline and Azithromycin group experienced side effects 22.6% and 20% respectively. Although there are few more side effects with Doxycycline in comparison with Azithromycin, 12 weeks treatment with Doxycycline gives better outcome in treatment of acne vulgaris and also is cheaper than Azithromycin. So Doxycycline can be the better alternative to Azithromycin and the treatment of choice for poor patients.

LIMITATION

The limitation of this study was small sample size, we did not explore the menstrual cycle of the female.

CONCLUSION

Both oral Azithromycin and Doxycycline when given for treatment of acne vulgaris the analysis showed good improvement after 6 weeks of treatment but there was no statistically significant difference in the improvement in both groups (p 0.771). However after 12 weeks, patient receiving Doxycycline showed statistically significant improvement (p 0.035) in comparison to the patients receiving Azithromycin. Though Doxycycline produces more side effects like nausea, headache, and photosensitivity whereas abdominal pain, nausea and diarrhoea is common in Azithromycin.

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