



A Comparative Study of Azithromycin Pulse Therapy with Minocycline in Acne Vulgaris.

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Abstract

Background: Acne vulgaris is a very common skin disease seen primarily in adolescents and young adults. Minocycline is a newly promoted drug in treating acne vulgaris. On the other hand it is assumed that, as a long term therapy with antibiotic having a long half-life like azithromycin can be very useful in increasing the compliance as well as efficacy in the treating acne vulgaris. But we have not enough comparative data regarding these issue. **Aim of the study:** The aim of this study was to compare the efficacy and safety of azithromycin pulse therapy with minocycline in treating acne vulgaris. **Methods:** This was comparative study which was conducted in the outpatient department of Cumilla Medical College Hospital, Cumilla, Bangladesh during the period from January 2018 to December 2018. In total 50 patients with moderate-to-moderately severe (Grade II and III) acne vulgaris were finalized as the study population. Patients were randomly assigned to two treatment groups. In Group A in total 25 patients were selected who received 50 mg minocycline twice a day along with 0.05% topical tretinoin for 3 months whereas in Group B another 25 patients were selected who received 500 mg azithromycin once a day for 3 days per week as pulse therapy along with 0.05% topical tretinoin for 3 months. All data were collected, processed, analyzed and disseminated by SPSS version 20 and MS Office program as per need. **Result:** In analyzing the changes of severity score of acne, in Group A at baseline 12%, 36% and 52% participants had the score point 2, 3 and 4 respectively whereas in final stage 64%, 32% and only 4% participants had the score point 1, 2 and 3 respectively. In Group B at baseline 8%, 32% and 60% participants had the score point 2, 3 and 4 respectively whereas in final stage 56%, 36% and the rest 8% participants had the score point 1, 2 and 3 respectively. In Group B between baseline and final score distribution the P value was found 0.064. We found in Group A among 24%, 8% cases diarrhea and nausea had been found respectively. However in Group B among 28%, 16% and 8% cases diarrhea, nausea and epigastric pain had been found respectively. Regarding the adverse events between both the groups we found a significant correlation where the P value was 0.048. **Conclusion:** We can conclude that, the efficacy of both the azithromycin pulse therapy and minocycline was found satisfactory. But according to the analysis of adverse events we found minocycline has got high pigmentation effect in treating acne vulgaris.

Keywords: Azithromycin, Minocycline, Acne Vulgaris, Pulse Therapy, Efficacy, Safety.

INTRODUCTION

Acne vulgaris is a very common skin disease seen primarily in adolescents and young adults. Minocycline is a newly promoted drug in Bangladesh treating acne vulgaris. On the other hand it is assumed that, as a long term therapy with antibiotic having a long half-life like azithromycin can be very useful in increasing the compliance as well as efficacy in the treating acne vulgaris. But we have not enough comparative data regarding these issue. Acne vulgaris is characterized by noninflammatory, open or closed comedones and inflammatory papules, pustules, and nodules. It results from androgen-induced increased sebum production, altered keratinization, inflammation, and bacterial colonization of hair follicles by *Propionibacterium acnes*.^[1] Acne is a complex disease with multifactorial pathogenesis and considerable variation in severity.^[2] Acne develops in the pilosebaceous unit, composed of epidermal cells lining the hair follicle and the sebaceous gland.^[3] Acne represents obstruction and inflammation of the sebaceous follicles, a subtype of pilosebaceous units.^[4] Antibiotic therapy has been an important part of acne management worldwide for the past 40 years, but acne is not an infection in the classic sense.^[5] The antibacterial effect of Azithromycin, like that of other macrolide antimicrobials, has been attributed to reversible binding to the 50S ribosomal subunit within the bacterial cell, with consequent inhibition of protein synthesis.^[6] There are tradition of using several topical agents in treating acne vulgaris also. There are many topical and systemic

modalities for acne treatment.^[7] But *P. acnes* possessed a vital place in the treatment arena of acne vulgaris. *P. acnes* is highly sensitive in vitro to a number of antimicrobial agents of different classes, including Macrolides, Tetracyclines, Penicillins, Clindamycin, Aminoglycosides, Cephalosporins, Trimethoprim, and Sulfonamides.^[7] The efficacy of all these agents depends on their ability to reach the lipid-rich environment of the pilosebaceous follicles where *P. acnes* proliferate. Thus, the choices of systemic antibiotic agents for treating acne include Tetracycline, Doxycycline, Minocycline, Erythromycin, Trimethoprim, and Azithromycin. Systemic treatments such as Azithromycin and Doxycycline are used routinely in clinical practice worldwide.^[8] Through this mechanism, Azithromycin exerts bacteriostatic, and sometimes bactericidal effects. It is not known if the antimicrobial activity of Azithromycin against nonbacterial species is attributed the same mechanism of action. Doxycycline inhibits bacterial protein synthesis by reversibly binding to the 30S ribosomal subunit and preventing the association of aminoacyl-tRNA with the bacterial ribosome.^[6] There have been previous studies comparing azithromycin with tetracyclines, such as doxycycline. Minocycline has also been studied and tested individually for treating acne. It has been found to be a good and effective choice of antibiotic for acne. However, on extensive review of literature, very few studies have been done to compare azithromycin with minocycline. This study had been conducted to collect comparative information regarding the efficacy and safety of azithromycin pulse

therapy and minocycline in treating acne vulgaris.

Objectives:

General Objective:

- To compare the efficacy of azithromycin pulse therapy with minocycline in acne vulgaris treatment.
- To compare the safety of azithromycin pulse therapy with minocycline in acne vulgaris treatment.

Specific Objective:

- To collect information regarding the adverse events among patients with acne vulgaris.

METHODOLOGY & MATERIALS

This was a prospective, randomized, comparative study which was the outpatient department of Cumilla Medical College Hospital, Cumilla, Bangladesh during the period from January 2018 to December 2018. In total 50 patients with moderate-to-moderately severe (Grade II and III) acne vulgaris attended the mentioned hospital were finalized as the study population. Patients were randomly assigned to two treatment groups. In Group A in total 25 patients were selected who received 50 mg minocycline twice a day along with 0.05% topical tretinoin for 3 months whereas in Group B another 25 patients were selected who received 500 mg azithromycin once a day for 3 days per week as pulse therapy along with 0.05% topical tretinoin for 3 months. The participants were recruited from both gender and the age range of the participants was 15 to 30 years. According to the exclusion criteria of this study, pregnant or lactating women,

patients taking topical treatment in last 2 weeks before the study or using of systemic antibiotic in the last 3 weeks before the study or using hormonal contraceptives, patients refused to consent or factors that limited the capacity of cooperation, patients with chronic underlying diseases/conditions and patients with known hypersensitivity to the study drug were excluded. A pre-designed questioner was used to collect all the necessary data. Patients who fulfilled the selection criteria were informed in detail about the study being done and about their contribution in the study. Where patients were not able to answer or were physically or mentally disable, informed consent was taken from the patient party. After taking written consent, the parameters including age, sex, duration of lesion, site of lesion, grade, relation to menstrual cycle, etc. as per questionnaire were obtained. Acne vulgaris was graded using a simple grading system taking into account the predominant lesion to grade acne, which classifies the acne vulgaris into four grades (Shelley and Kligman, 1956)⁹:

Grade 1: Comedones and occasional small cysts confined to the face.

Grade 2: Comedones with occasional pustules and small cysts confined to the face.

Grade 3: Many comedones and small and large inflammatory papules and pustules, more extensive but confined to the face.

Grade 4: Many comedones and deep lesions tending to coalesce and canalize, and involving the face and the upper aspects of the trunk.

NB.: In this study, additionally 'Grade Zero' was used at the end of treatment and during the follow-up and defined as nonexistence of the lesions.



All data were collected, processed, analyzed and disseminated by SPSS version 20 and MS Office program as per need.

RESULT

In this study in Group A the highest number of patients were found from 21-25 years' age group which was 48%. Then 36% were from 15-20 years' age group and the rest 16% were from 26-30 years' age group. On the other hand, in Group B the highest number of patients were found from 21-25 years' age group also and it was 52%. Then 36% were from 15-20 years' age group and the rest 12% were from 26-30 years' age group. We found a significant correlation between the groups in age distribution where the P value was 0.018. The mean age of Group A participants was 23.62 years whereas it was 23.87 years in Group B. In analyzing the gender of the participants we observed in Group A 40% participants were male and 60% were female whereas in Group B 36% participants were male and 64% were female. So in both the groups female were dominating in number. In Group A 40%, 24%, 16%, 8% and 12% participants were student, housewife, service holder, laborer and persons involved in other professions respectively. On the other hand, in Group B 36%, 24%, 24%, 8% and the rest another 8% participants were student,

housewife, service holder, laborer and persons involved in other professions respectively. In analyzing the changes of severity score of acne among the participants of both groups we found, in Group A at baseline 12%, 36% and 52% participants had the score point 2, 3 and 4 respectively whereas in final stage 64%, 32% and only 4% participants had the score point 1, 2 and 3 respectively. In Group A between baseline and final score distribution the P value was found 0.053. On the other hand, in Group B at baseline 8%, 32% and 60% participants had the score point 2, 3 and 4 respectively whereas in final stage 56%, 36% and the rest 8% participants had the score point 1, 2 and 3 respectively. In Group B between baseline and final score distribution the P value was found 0.064. In analyzing the adverse event during the treatment tenure we found in Group A among 24%, 8% cases diarrhea and nausea had been found respectively. In this group we observed not any case with epigastric pain which was found in another group. However in Group B among 28%, 16% and 8% cases diarrhea, nausea and epigastric pain had been found respectively. Regarding the adverse events between both the groups we found a significant correlation where the P value was 0.048.

Table I: Demographic characteristics of the study population (n=50)

| Characteristics | Group A | | Group B | | p-value |
|-----------------|---------|----|---------|----|---------|
| | No | % | No. | % | |
| Age in year | | | | | |
| 15-20 | 9 | 36 | 9 | 36 | 0.018 |
| 21-25 | 12 | 48 | 13 | 52 | |
| 26-30 | 4 | 16 | 3 | 12 | |
| Gender | | | | | |



| | | | | | |
|------------|----|----|----|----|-------|
| Male | 10 | 40 | 9 | 36 | |
| Female | 15 | 60 | 16 | 64 | |
| Occupation | | | | | |
| Student | 10 | 40 | 9 | 36 | 0.026 |
| Housewives | 6 | 24 | 6 | 24 | |
| Service | 4 | 16 | 6 | 24 | |
| Laborer | 2 | 8 | 2 | 8 | |
| Others | 3 | 12 | 2 | 8 | |

Table II:Severity score⁹ distribution of acne among participants of both groups (n=50)

| Score | Group A | | | | Group B | | | |
|---------|-----------|----|-------|---|-----------|----|-------|----|
| | Baselin e | | Final | | Baselin e | | Final | |
| | n | % | n | % | n | % | n | % |
| 1 | 0 | 0 | 1 | 6 | 0 | 0 | 14 | 56 |
| 2 | 3 | 12 | 8 | 3 | 2 | 8 | 9 | 36 |
| 3 | 9 | 36 | 1 | 4 | 8 | 32 | 2 | 8 |
| 4 | 13 | 52 | 0 | 0 | 15 | 60 | 0 | 0 |
| P Value | 0.053 | | | | 0.064 | | | |

Table III:Distribution of adverse events among participants of both groups (n=50)

| Adverse event | Group A | | Group B | | P value |
|-----------------|---------|----|---------|----|---------|
| | n | % | n | % | |
| Diarrhoea | 6 | 24 | 7 | 28 | 0.048 |
| Nausea | 2 | 8 | 4 | 16 | |
| Epigastric pain | 0 | 0 | 2 | 8 | |
| Pigmentation | 1 | 4 | 0 | 0 | |
| Total | 9 | 36 | 13 | 52 | |

DISCUSSION

The aim of this study was to compare the efficacy and safety of azithromycin pulse therapy with minocycline in treating acne vulgaris. Erythromycin is the first macrolide used in the treatment of acne vulgaris. It has been used much less frequently owing to the GI side effects.^[10] Erythromycin also has a short half-life requiring frequent administration. There are a lot of known drug interactions associated with it. For this reason, the newer

macrolides such as azithromycin began to be used more frequently. Azithromycin has fewer GI side effects, longer half-life, and good tissue penetration in treatment procedure. The extensive distribution of azithromycin in the tissues allows recommendation of pulse-dose regimen to improve the compliance. Azithromycin is an azalide in nature of the macrolide group of antibiotics. It has an azamethyl substitution in the macrolide ring. The addition of the second amine group



resulted in important advantages over erythromycin, including greater tissue penetration and an extended half-life.^[11] Azithromycin inhibits protein synthesis by binding to 50S ribosomal subunit and preventing translocation. Azithromycin is primarily a bacteriostatic drug, but in higher concentration can be bactericidal. The most common treatment-related side effects involve the GI tract, including diarrhea, nausea, and abdominal cramping.^[12] On the other hand, minocycline, a semi-synthetic, second-generation tetracycline, has a better pharmacokinetic profile, and compared with doxycycline, it is not phototoxic.^[13] Minocycline can be taken more conveniently as once or twice daily dose compared with the generally more frequent dosing of other tetracyclines. It being lipophilic achieves greater tissue concentration and is thought to be more effective than doxycycline in acne, a view held by the Global Alliance. Tetracyclines are bacteriostatic in nature which are considered broad-spectrum antibiotics because they are active against a wide range of aerobic and anaerobic Gram-positive and Gram-negative bacteria. The mechanism of action behind the antibiotic properties of tetracyclines is mainly related to their ability to bind to the bacterial 30S ribosomal subunit and inhibition of protein synthesis. The most common known side effects of minocycline are nausea, vertigo, and mild dizziness.^[14] Some systemic side effects such as GI disturbances, tooth discoloration, enamel hypoplasia, autoimmune hepatitis, and drug hypersensitivity syndrome may occur. Many studies have shown macrolides, especially azithromycin, to be very effective for the treatment of acne vulgaris. There have been previous studies comparing azithromycin with tetracyclines,

likedoxycycline. However, on extensive review of literature, very few studies have been done to compare azithromycin with minocycline. Minocycline has been studied and tested individually for treating acne. It has been found to be a good and effective choice of antibiotic for acne. Knowing that minocycline has a lot of advantages over other tetracyclines, it was imperative to study whether it is superior to azithromycin in the treatment of acne. In our study, in analyzing the changes of severity score of acne, in Group A (Minocycline) at baseline 12%, 36% and 52% participants had the score point 2, 3 and 4 respectively whereas in final stage 64%, 32% and only 4% participants had the score point 1, 2 and 3 respectively. In Group B (Azithromycin) at baseline 8%, 32% and 60% participants had the score point 2, 3 and 4 respectively whereas in final stage 56%, 36% and the rest 8% participants had the score point 1, 2 and 3 respectively. In Group B between baseline and final score distribution the P value was found 0.064. We found in Group A among 24%, 8% cases diarrhea and nausea had been found respectively. However in Group B among 28%, 16% and 8% cases diarrhea, nausea and epigastric pain had been found respectively. Through this study we observed, the efficacy of both the azithromycin pulse therapy and minocycline was found satisfactory. But according to the regression analysis of adverse events we found minocycline is safer than azithromycin pulse therapy in treating acne vulgaris.

CONCLUSION

We can conclude that, the efficacy of both the azithromycin pulse therapy and minocycline



was found satisfactory. But according to the analysis of adverse events we found minocycline has got high pigmentation effect in treating acne vulgaris. For that reason, patient compliance of pulse therapy of azithromycin had been approved by most of the patients of azithromycin pulse therapy

group. But this was a single centered study with a small sized sample. So the findings of this study may not reflect the exact scenario of the whole country. For getting more specific findings we would like to recommend for conducting more studies regarding the same issue.

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