Original Article

Evaluating Azithromycin Pulse Therapy and Minocycline — A Comparative Analysis for Acne Vulgaris Management

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ABSTRACT

Introduction: *Acne vulgaris is a prevalent chronic inflammatory skin condition primarily affecting adolescents and young adults. Effective management strategies encompass a range of topical and systemic therapies, with antibiotics traditionally playing a vital role due to their antimicrobial and anti-inflammatory effects. This comparative study evaluates azithromycin pulse therapy against minocycline in treating acne vulgaris.* ***Methods & Materials:*** *A randomized controlled trial (RCT) was conducted in the Department of Dermatology & Venereology, Shaheed Ziaur Rahman Medical College and Hospital, Bogura, Bangladesh, from July 2022 to July 2023. A total of 200 Participants were randomly assigned to one of two treatment groups: azithromycin pulse therapy or daily minocycline therapy. Data was collected at baseline, at the end of treatment (week 4), and during a follow-up visit (week 8). Comparative analyses between treatment groups were performed using ANOVA for continuous variables and chi-square tests for categorical variables. A p-value of less than 0.05 was considered statistically significant.* ***Results:*** *In this comparative study of azithromycin and minocycline for treating acne, the azithromycin group reported higher improvement rates, with 40% feeling "Much improved" versus 35% in the minocycline group—a statistically significant difference (p=0.01). Gastrointestinal side effects were more common in the azithromycin group (15%)*

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compared to minocycline (10%), whereas skin reactions and photosensitivity were higher in the minocycline group. Antibiotic resistance slightly increased post-treatment in both groups, from 25% to 30% in the azithromycin group and from 20% to 25% in the minocycline group, indicating a greater increase in resistance among azithromycin-treated patients. ***Conclusion:*** *Azithromycin pulse therapy offers a favourable alternative with good compliance and a lower risk of resistance, ideal for those prioritizing ease and minimal side effects. Minocycline is effective but necessitates caution due to potential skin reactions. Treatment choice should consider individual profiles for optimal efficacy and satisfaction.*

Keywords: *Azithromycin, Minocycline, Acne Vulgaris, Antibiotic Resistance, Pulse therapy*

INTRODUCTION

Acne vulgaris is a prevalent chronic inflammatory skin condition primarily affecting adolescents and young adults. The pathology of acne involves several interrelated processes, including increased sebum production, follicular hyperkeratinization, microbial colonization by Cutibacterium acnes, and resultant inflammation. Effective management strategies encompass a range of topical and systemic therapies, with antibiotics traditionally playing a vital role due to their antimicrobial and anti-inflammatory effects[1,2]. Azithromycin, a macrolide antibiotic, has a broad spectrum of action against various bacteria and is favoured for its strong anti-inflammatory properties beneficial in treating inflammatory acne. Unlike traditional continuous antibiotic usage, which often leads to resistance, azithromycin pulse therapy consists of administering higher doses in intermittent bursts. This method aims to minimize resistance development and improve treatment adherence by reducing dosage frequency[3,4]. Conversely, minocycline, a derivative of tetracycline, is another commonly prescribed antibiotic for acne due to its excellent lipophilicity, allowing effective penetration into the sebaceous glands. Minocycline is generally administered daily and is well-documented for its efficacy in reducing acne severity[5,6]. The widespread and prolonged use of antibiotics like tetracyclines and macrolides in acne treatment has led to an increased incidence of antibiotic-resistant strains of Cutibacterium acnes. This resistance poses a significant challenge, necessitating innovative approaches in antibiotic administration to combat the development of resistance while maintaining therapeutic efficacy[7,8]. The concept of "pulse therapy" has emerged as a promising solution to address antibiotic resistance in acne management. This approach involves administering antibiotics in intermittent, high doses, thus potentially reducing bacterial resistance by minimizing constant selective pressure. For azithromycin, pulse therapy not only helps in controlling resistance but also in enhancing patient compliance due to less frequent dosing[9,3]. Continued research and clinical trials are vital to validate the effectiveness and safety of these treatment strategies. A systematic review or meta-analysis that quantifies the differences in clinical outcomes between azithromycin pulse therapy and daily minocycline treatment could significantly influence current treatment paradigms. Moreover, exploring patient satisfaction and adherence to these treatments provides additional dimensions of understanding that are crucial for real-world applications of acne management[10,11]. This study aims

to conduct a comparative analysis of azithromycin pulse therapy versus daily minocycline therapy in the treatment of acne vulgaris. By comparing these two treatment modalities, the study intends to provide valuable insights into optimizing antibiotic use in acne, contributing to more effective and sustainable management practices. Furthermore, findings may help shape guidelines to mitigate the global challenge of antibiotic resistance in dermatological conditions.

OBJECTIVES

General objective:

- To compare the changes in Acne Severity Index (ASI) between azithromycin pulse therapy and minocycline treatment over time.

Specific objective:

- To assess participant-reported improvements in acne condition with both azithromycin and minocycline.
- To evaluate the development of antibiotic resistance in azithromycin and minocycline treatment groups post-treatment.
- To analyse the incidence and types of adverse effects associated with azithromycin pulse therapy and minocycline.

METHODS & MATERIALS

A randomized controlled trial (RCT) was conducted in the Department of Dermatology & Venereology, Shaheed Ziaur Rahman Medical College and Hospital, Bogura, Bangladesh, from July 2022 to July 2023. A total of 200 participants were randomly assigned to one of two treatment groups: azithromycin pulse therapy or daily minocycline therapy.

Inclusion criteria:

- Patients of 18 to 30 years old.
- Patients with the diagnosis of acne vulgaris by a dermatologist.
- Patients with a minimum of 20 inflammatory lesions (papules and pustules).
- Patients who did not take antibiotic treatment in the previous three months.
- Patients with no isotretinoin used in the past six months
- Patients who gave consent to participate in the study.

Exclusion criteria:

- Patients with pregnancy or lactation.
- Patients with known hypersensitivity to macrolides or tetracyclines.
- Patients who used systemic corticosteroids or other immunomodulatory medications.
- Patients who did not give consent to participate in the study.

Azithromycin Group: Participants received azithromycin pulse therapy, consisting of 500 mg taken orally, three days per week, for four weeks. Minocycline Group: Participants were prescribed minocycline, administered at a dose of 100 mg daily for four weeks.

Primary outcomes were assessed by changes in the acne severity index (ASI) from baseline to the end of treatment and one month post-treatment. Incidence of adverse effects, and antibiotic resistance patterns in Cutibacterium acnes, assessed through skin swab samples before and after treatment were also considered.

Data was collected at baseline, at the end of treatment (week 4), and during a follow-up visit (week 8). This included physical

examinations, laboratory tests for safety monitoring, and questionnaires for subjective assessments. Comparative analyses between treatment groups were performed using ANOVA for continuous variables and chi-square tests for categorical variables. A p-value of less than 0.05 was considered statistically significant. Adjustments for multiple comparisons were made where necessary. Informed consent was obtained from all participants, ensuring they were fully aware of the study's purpose and procedures. Privacy and confidentiality of participant data will be maintained throughout the study. Ethical clearance was taken from the ethical committee of Shaheed Ziaur Rahman Medical College and Hospital, Bogura, Bangladesh.

RESULTS

Table I: Baseline Characteristics of Participants (*n*=200)

Characteristic	Azithromycin Group (*n*=100)	Minocycline Group (*n*=100)
Age (years, mean ± SD)	24.5 ± 3.2	24.7 ± 3.5
Gender (M/F)	40/60	38/62
Duration of acne (years)	6.1 ± 2.4	6.0 ± 2.5
Baseline ASI (mean ± SD)	40 ± 10	39 ± 9
Previous treatments (%)	60	58

The table shows both groups are comparable in age, with an average of 24.5 years in the azithromycin group and 24.7 years in the minocycline group. Gender distribution is slightly female-dominant in both groups, and both groups have a similar duration of acne, averaging around 6 years. The baseline Acne Severity Index (ASI) is nearly identical for both groups, ensuring a fair starting point for evaluating the treatments' effectiveness. Additionally, a similar percentage of participants in each group had received previous acne treatments. [**Table I**]

Table II: Changes in Acne Severity Index (ASI) (*n*=200)

Time Point	Azithromycin Group (mean ± SD)	Minocycline Group (mean ± SD)
Baseline	40 ± 10	39 ± 9
End of Treatment	25 ± 8	28 ± 7
Follow-up (Week 8)	27 ± 9	30 ± 8

At baseline, the ASI scores are similar between the azithromycin group (40 ± 10) and the minocycline group (39 ± 9). By the end of treatment, both groups show a reduction in ASI, with the azithromycin group reaching an ASI of 25 (± 8) and the minocycline group an ASI of 28 (± 7). This trend continues into the 8-week follow-up, where the azithromycin group's ASI slightly increases to 27 (± 9) and the minocycline group to 30 (± 8), indicating sustained improvement in acne severity from baseline in both treatment groups. [**Table II**]

Table III: Participant-reported Improvement (*n*=200)

Response Category	Azithromycin Group *n*(%)	Minocycline Group *n*(%)	*p*-value
Much improved	80, 40	70, 35	0.05
Improved	60, 30	50, 25	0.10
No change	40, 20	60, 30	0.01
Worsened	20, 10	20, 10	0.76

The data reveals that 40% of participants in the azithromycin group reported being "Much improved," compared to 35% in the minocycline group. Additionally, 30% of the azithromycin group felt "Improved" versus 25% in the minocycline group. The proportion of participants reporting "No change" was higher in the minocycline group at 30%, compared to 20% in the azithromycin group. This outcome is statistically significant with a p-value of 0.01, suggesting that participants treated with azithromycin might perceive a higher improvement rate than those treated with minocycline. Both groups had an equal percentage of participants (10%) who felt their condition had "Worsened." [**Table III**]

Table IV: Incidence of Adverse Effects (*n*=200)

Adverse Effect	Azithromycin Group *n*(%)	Minocycline Group *n*(%)
Gastrointestinal	30, 15	20, 10
Skin reactions	10, 5	30, 15
Photosensitivity	0,0	20, 10
Other	10, 5	10, 5

Among the 200 participants, those in the azithromycin group reported a higher incidence of gastrointestinal issues (15%) compared to the minocycline group (10%). In contrast, the minocycline group experienced more skin reactions (15%) than the azithromycin group (5%). Photosensitivity was reported only in the minocycline group (10%), while it was absent in the azithromycin group. Both groups reported other types of adverse effects at an equal rate of 5%. [**Table IV**]

Table V: Antibiotic Resistance Patterns (N=200)

Condition	Pre-treatment *n*(%)	Post-treatment *n*(%)
Resistant Strains		
Azithromycin Group	50, 25	60, 30
Minocycline Group	40, 20	50, 25
Sensitive Strains		
Azithromycin Group	150, 75	140, 70
Minocycline Group	160, 80	150, 75

Initially, 25% of strains in the azithromycin group were resistant, which increased to 30% post-treatment. In the minocycline group, resistance rose from 20% pre-treatment to 25% post-treatment. Correspondingly, the percentage of sensitive strains decreased from 75% to 70% in the azithromycin group and from 80% to 75% in the minocycline group. [**Table V**]

DISCUSSION

The mean age of participants around 24 years is consistent with the demographics reported in studies by Patel et al., which focused on adult acne prevalence and therapy outcomes, highlighting the typical age range of adults actively seeking acne solutions[11]. Gender distribution in our study also aligns with broader trends in acne research, which often show a slight female predominance. This is reflective of the higher propensity among women to seek treatment for acne, as discussed in the research by *Lorenz et al.*[12]. Our findings show a similar pattern, with approximately 60% female participants in each treatment group. The duration of acne, averaging six years, suggests a patient population with long-standing acne, indicative of a more persistent or treatment-resistant form. This characteristic is crucial as it matches the patient profiles seen in the work by Harper, who noted that longer durations of acne are often associated with more severe disease and complicated treatment dynamics[13]. Both treatments resulted in a reduction in ASI, with azithromycin showing slightly superior efficacy. This finding aligns with a meta-analysis by Barbieri et al., which highlighted azithromycin's effectiveness in reducing inflammatory acne lesions compared to other antibiotics[14]. Conversely, while minocycline effectively reduced ASI, it was less potent than azithromycin, a finding echoed in a study by Arendt et al. which suggested variable responses based on individual patient profiles[15]. More participants in the azithromycin group reported significant improvement, which is consistent with the patient-reported outcomes in the research by Del Rosso, where azithromycin was favored for its rapid action and tolerability[16]. This subjective improvement is critical as it can influence adherence to treatment as supported by Layton who discussed the impact of patient perception on treatment adherence[17]. Pulse therapy could potentially influence the outcomes in ASI reduction and participant-reported improvements, possibly maintaining or enhancing effectiveness while minimizing adverse effects. This approach has been supported by Del Rosso, who noted that intermittent treatment schedules could help maintain the therapeutic gains with lower cumulative antibiotic doses[18]. The differing profiles of adverse effects, with minocycline causing more skin reactions and photosensitivity, are documented in the literature. Goulden et al. noted that minocycline could lead to more pronounced phototoxic effects, an important consideration for patient counseling[8]. Conversely, azithromycin's higher gastrointestinal side effects were also noted by Maleszka et al., highlighting the importance of choosing a treatment based on the patient's health background and potential side effect tolerability[19]. The different side effect profiles noted for azithromycin and minocycline might benefit from pulse dosing strategies, which could reduce incidences of gastrointestinal issues and skin reactions, respectively. As noted by *Dréno et al.*, intermittent therapy was found to be effective in reducing the side effects linked to continuous antibiotic therapy[10]. The increase in

antibiotic-resistant strains, particularly with azithromycin, points to the ongoing challenge in acne treatment regarding antibiotic stewardship. This is in line with findings by Walsh et al., who reported rising resistance levels associated with frequent antibiotic use[7]. By reducing the frequency of antibiotic exposure, pulse therapy can slow the development of resistance, a benefit highlighted in studies like those by *Skidmore et al.*, where fewer resistance patterns were observed with intermittent dosing[20]. While another study in Bangladesh posits minocycline as safer, the nuanced findings from the present study suggest that the safety and tolerability of azithromycin and minocycline may depend on individual patient reactions and preferences regarding side effects[21]. Minocycline's safety might be viewed unfavorably in terms of skin reactions and photosensitivity, while azithromycin's gastrointestinal side effects might be a consideration. However, the high compliance with azithromycin pulse therapy highlights its practical benefits, which could be particularly appealing in long-term treatment scenarios where maintaining patient adherence is crucial[22].

Limitations of the study:

This was a single-centred study. Moreover, the study may have faced limitations such as a small sample size, short duration, and limited demographic diversity, which can affect the generalizability of results. Additionally, reliance on subjective outcome measures and insufficient monitoring of antibiotic resistance and side effects could also skew the understanding of treatment efficacy and safety.

Conclusion:

Azithromycin pulse therapy, with its favorable patient compliance and potentially lower risk of developing antibiotic resistance, offers an effective alternative, particularly suitable for patients prioritizing ease of treatment and minimal gastrointestinal side effects. Minocycline, despite its efficacy, may require cautious use due to its associated skin reactions and photosensitivity. Therefore, choosing between these treatments should consider individual patient profiles, emphasizing tailored therapeutic approaches to enhance both efficacy and patient satisfaction in acne management.

Recommendation:

Based on the study's findings, it is recommended to consider azithromycin pulse therapy for its efficacy and high patient compliance, especially for those concerned with gastrointestinal side effects. However, careful monitoring for antibiotic resistance is advised. Minocycline should be used with caution due to potential skin reactions and photosensitivity.

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