Section: Dermatology

Original Research Article

COMPARISON OF ORAL AZITHROMYCIN PULSE THERAPY VERSUS DAILY DOXYCYCLINE IN THE TREATMENT OF ACNE VULGARIS

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Abstract

Background: Acne vulgaris is a common, self-limiting, inflammatory disease of the pilosebaceous unit, presenting with pleomorphic lesions like comedones, papules, nodules, and in severe cases cysts, that affects individuals of various age groups causing physical and psychological distress. Antibiotics are frequently used as a mainstay of treatment for moderate to severe cases of acne. The aim & objective is to compare the efficacy, safety, and tolerability of oral azithromycin pulse therapy versus daily doxycycline in the treatment of acne vulgaris **Materials and Methods:** An open randomized controlled trial was conducted on 80 patients diagnosed with moderate to severe acne vulgaris over 6 months. In the group A azithromycin 500mg was prescribed for 3 consecutive days in a week. The group B was given doxycycline 100 mg daily. Topical clindamycin was prescribed to all the patients. Clinical assessment was done at 4-week intervals for both groups up to 12 weeks. Michaelsson Acne Severity Index was followed for the assessment of outcome measures. **Result:** In Group A (Azithromycin) 90% of patients achieved good response and 10% achieved moderate response and in Group B (Doxycycline)50% achieved good and 50% achieved moderate response (p=0.001). No severe adverse effect was recorded except nausea, diarrhea, abdominal pain, and itching(p>0.05). **Conclusion:** Azithromycin pulse therapy is more effective with fewer side effects than daily doxycycline in treating acne vulgaris.

INTRODUCTION

Acne vulgaris a common chronic, inflammatory disorder of the pilosebaceous unit, generally manifests in adolescents with polymorphic lesions like comedones, papules, pustules, nodules, and cysts. When the condition isn't treated duly it can lead to scarring.[1] Acne affects the skin with a greater number of oil glands including the face, chest, and back. Pathogenesis of acne is due to increased sebum secretion, follicular hyperkeratinisation, colonization of pilosebaceous glands by propionic bacterium, and inflammation.[2]

Acne can be treated with medications that are either applied directly to the skin or taken orally. Topical treatments such as benzoyl peroxide, antibiotics, and retinoids are usually the first choice for mild to moderate acne. On the other hand, systemic treatments like oral antibiotics, oral retinoids, and hormonal remedies are typically used in combination with a topical agent for moderate to severe acne.[3,4]

Azithromycin is a type of antimicrobial drug called a macrolide. It is structurally similar to erythromycin but has improved pharmacokinetic properties and a wider range of uses. Azithromycin is quickly absorbed and released into the bloodstream, and has a long half-life in tissues, which means it can be administered less frequently.[5] The most common side effect of azithromycin is mild gastrointestinal discomfort.

Doxycycline is a first-line anti-acne antibiotic. Gastrointestinal side effects such as nausea, vomiting, and diarrhea are common during doxycycline treatment. This medication can also cause inflammation or ulcers in the esophagus, known as pill esophagitis. Also, there can be permanent tooth discoloration in individuals with developing teeth.

Comparative clinical trials have shown that azithromycin has improved pharmacokinetic

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properties and a high tolerability profile and efficacy against P. acnes. Its rationale for use in acne has been examined and found to be effective and superior to doxycycline.[6]

Therefore, we conducted a study to compare the efficacy and safety of oral azithromycin pulse therapy, 500mg once daily for 3 consecutive days in a week versus oral doxycycline 100mg daily for 12 weeks.

MATERIALS AND METHODS

This study is an open randomized control trial conducted to compare the efficacy and safety of oral azithromycin versus oral doxycycline in the treatment of acne vulgaris.

Patients, who visited the outpatient department of the Department of Dermatology, at Varun Arjun Medical College & Rohailkhand Hospital, Shahjahanpur, Uttar Pradesh diagnosed with acne vulgaris were the source of samples in the study. The study duration was 12 weeks and the study period was from April 2023 to September 2023.

Subject Selection Criteria

Inclusion Criteria

- Patients diagnosed with acne vulgaris at the Department of Dermatology outpatient department at VAMCRH, Shahjahanpur, Uttar Pradesh.
- Participant's willingness to participate in the study and provide informed consent.
- Patients of both sexes, aged more than 12 years.

Exclusion Criteria

- Persons having hypersensitivity to azithromycin or doxycycline.
- Pregnancy or lactation.
- Patient suffering from any concomitant systemic illness.
- Female patients who are on oral contraceptive pills.
- Persons working under direct sunlight.

After informed consent, complete history and general and dermatological examinations were done for all enrolled patients. Only patients who met the specified inclusion and exclusion criteria were chosen for the study. On clinical examination, lesions were graded according to the Michaelsson Acne Severity Index by counting the number of comedones, papules, pustules, infiltrated nodules, and cysts.

Michaelsson Acne Severity Index is described as 0.5 for comedones, 1.0 for papules, 2.0 for pustules, 3.0 for nodules and infiltrates, and 4.0 for cystic lesions. The total severity score was calculated by multiplying each type of lesion with the severity index and adding them.[7]

Drug Dosage

Group-A: (40 patients) Oral Azithromycin 500 mg for 3 consecutive days in a week for 8 weeks.

Group-B (40 patients) Oral Doxycycline 100 mg daily for 8 weeks.

Five scheduled visits were carried out during the study period– Baseline visit, at the end of the 4th week, at the end of the 8th week, visit at the end of the 12th week, and post-treatment follow-up. The response to treatment was evaluated during each follow-up visit. During visits checklist for side effects attributable to either drug nausea, vomiting, diarrhea, headache, rash, photosensitivity, itching, dizziness, and pigmentation were also noted and recorded.

The Michaelsson Acne Severity Index was used to assess the severity of acne at every visit. Photos were taken before treatment (baseline) and during each subsequent visit. The assessment was based on the percentage decrease in the total score from baseline. An 80% or more reduction was considered good, 50-79% was moderate, 20-49% was poor, and less than 20% reduction was labeled as no response.[8]

RESULTS

Of 80 patients, 40 were in the azithromycin group and 40 in the doxycycline group 44 (55%) were females and 36(45%) were males.

Table 1: Demonstrating distribution of patients based on age

	Groups		P value
	Group A	Group B	
Mean Age (years)	20.33± 5.16	20.30± 4.09	0.978

[Table 2] Records the distribution of various grades of acne vulgaris before and after the 4th, 8th, and 12th week of treatment with either Group A (Azithromycin) or Group B (Doxycycline) for acne vulgaris.

Table 2: Distribution of various grades

Group A					Group B			
Baseline		4th week	8th week	12th week	Baseline	4th week	8th week	12th week
Grade I	10	12	14	16	08	14	15	18
Grade II	13	14	18	10	10	12	14	15
Grade III	8	10	04	03	14	08	06	04
Grade IV	9	04	02	01	08	06	05	03

Before treatment, Group A's mean total acne score was 78.87 ± 29.14, compared to 73.88 ± 23.33 for Group B. At the first follow-up, the total acne score for Group A was 54.77 ± 26.30, while for Group B it was 55.05 ± 21.64. At the second follow-up, the total acne score for Group A was 34.48 ± 20.94, and for Group B it was 39.70 ± 19.57. At the third follow-up, the total acne score for Group A was 18.52 ± 12.44, whereas for Group B it was 27.60 ± 17.31. At the

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post-treatment follow-up, the total acne score for Group A was 8.75 ± 7.34, and for Group B it was 17.40 ± 4.21.
[Figure 1] Line chart that displays the total acne score of study participants at different follow-up visits.

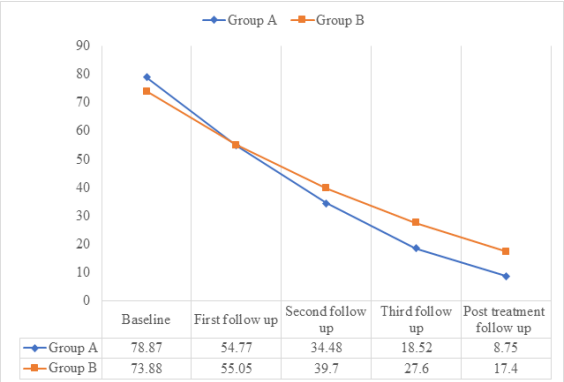

Figure 1: Total acne score of different follow-ups of study participants

Out of 80 patients, In Group A (Azithromycin) no response in 3 (7.5%), mild response in 4 (10%), moderate response in 8 (20%), good response in 20 (50%), and excellent response in 5 (12.5%). in Group B (Doxycycline) no response in 6 (15%), mild response in 11 (27.5%), moderate response in 7 (17.5%), good in 13 (32.5%), and excellent in 3 (7.5%).
[Figure 2] Shows the level of response to treatment in different groups.

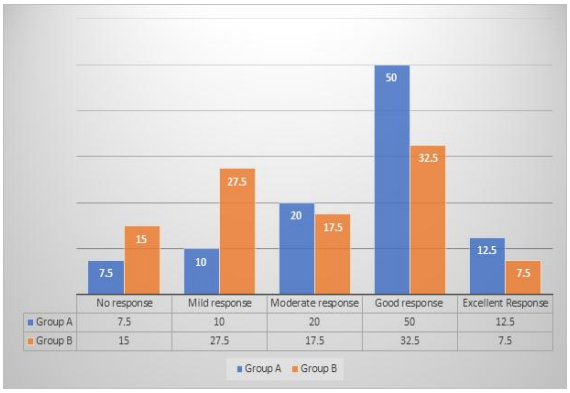

Figure 2: Response level upon azithromycin and doxycycline treatment

The results for certain patients, featuring clinical images before and after treatment, are depicted in Figures 3 and 4 for Group A, and Figures 5 and 6 for Group B, respectively.

Figure 3: Depicts the regression of lesions from Grade II to Grade I over a 4-week duration

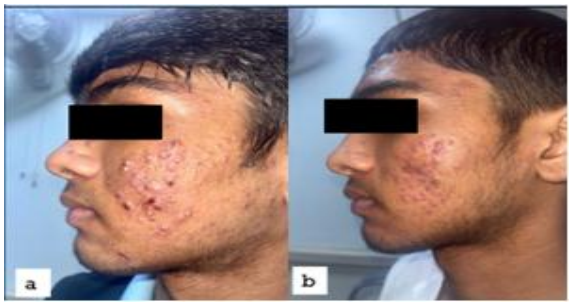

Figure 4: Illustrates the regression of lesions from Grade III to Grade I over an 8-week duration

Figure 5: Illustrates the regression of Grade IV lesions to Grade III in 12 weeks

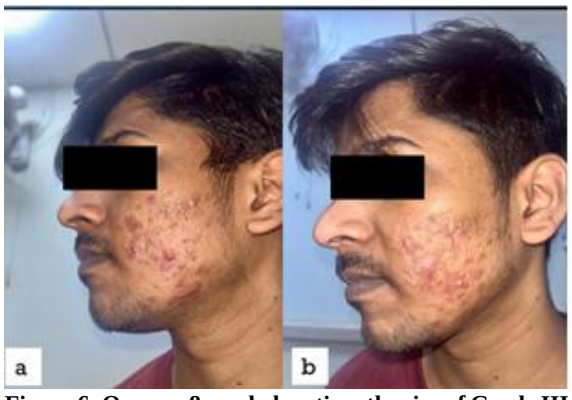

Figure 6: Over an 8-week duration, the size of Grade III lesions decreased to Grade II

SIDE EFFECTS

Regarding side effects, in Group A (Azithromycin), 80% of participants had no side effects, while 20%

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experienced gastrointestinal side effects. Out of those, 9% reported diarrhea and 11% had abdominal pain. In Group B (Doxycycline), 54% of participants had no side effects, while 46% experienced gastrointestinal side effects. Out of those, 10% reported nausea, 19% had diarrhea, and 17% experienced abdominal pain.

Fig:7 Shows the frequency of GIT side effects in participants.

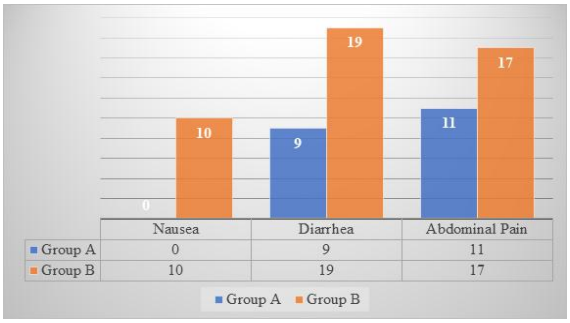

Figure 7: gastrointestinal side effects in study subjects

DISCUSSION

Acne vulgaris is a widespread condition that affects around 95% of adolescents and can cause psychological distress and lasting scarring.[9] Since the 1980s, oral antibiotics have been commonly used to treat acne. These antibiotics work by reducing the amount of p. acnes bacteria in the hair follicles and providing anti-inflammatory and immunomodulatory effects.[10]

A recent study was conducted on 80 patients to compare the effectiveness of pulse dose Azithromycin (500mg for three consecutive days in a week) versus daily doxycycline (100mg) in treating acne vulgaris. The study subjects had an average age of 26.7 ± 6.2 years, which is consistent with another acne study by Kane et al in 2007.[11] Various studies have examined the effectiveness and potential side effects of both azithromycin and doxycycline for treating acne. Gruber et al conducted a study in Croatian patients and found that treating acne vulgaris with azithromycin or minocycline resulted in satisfactory clinical response, with no significant differences in efficacy or tolerability.[12]

During the follow-up visits, it was observed that both groups experienced a significant reduction in acne grades compared to the baseline. This indicates that both drugs are effective in treating acne vulgaris. However, toward the end of the study, there were more patients with grade III (10%) and grade IV (7.5%) acne in the Doxycycline group (Group B) compared to the Azithromycin group (Group A) with grade III (7.5%) and grade IV (2.5%). This suggests that Azithromycin is more efficient in reducing acne's severity than Doxycycline.

Group A showed a significantly higher acne reduction (p=0.001) than Group B, with a mean percent reduction of acne score from baseline to treatment follow-up of 89.91 ± 7.76 for Group A and 79.03 ± 13.12 for Group B.

A further comparison of responses in Group A and Group B revealed that Azithromycin pulse therapy is more effective in achieving improvement.

Italian acne patients were studied to determine the safety and effectiveness of azithromycin. In one study, 500mg of azithromycin was given thrice weekly for 8 weeks, resulting in excellent patient compliance and promising results.[13] Another study found that 500mg of azithromycin thrice weekly for 12 weeks was a safe and effective treatment for moderate acne vulgaris in Italian patients, with only a few side effects such as diarrhea and abdominal pain.[14]

In a non-comparative study conducted among Brazilian acne patients, three monthly pulses of azithromycin 500mg for 3 consecutive days were given. The study concluded that azithromycin was safe and well-tolerated, with good patient adherence to the treatment. However, gastrointestinal and central nervous system adverse events were reported.[15]

In the present study, Group A and Group B only showed gastrointestinal side effects.

A comparison of the effectiveness of azithromycin monthly pulse therapy and daily doxycycline treatment for acne vulgaris in Chandigarh patients showed that the monthly dose of azithromycin was more effective than daily doxycycline doses.[16] In Turkish acne patients, both azithromycin and doxycycline antibiotics were found to be equally effective in treating acne, but both groups experienced side effects. Specifically, azithromycin was associated with diarrhea while doxycycline caused photosensitivity.[17]

CONCLUSION

Our research indicates that both azithromycin and doxycycline effectively reduce acne. However, towards the end of the study, we observed a lower number of grade III and IV patients in Group A (azithromycin) compared to Group B (doxycycline), which suggests that azithromycin is more effective at reducing the severity of acne than doxycycline. Additionally, the proportion of good and excellent responses was higher with azithromycin. Therefore, we conclude that Azithromycin pulse therapy 500mg daily for three consecutive days a week is a more effective and safer treatment option for acne vulgaris than daily doxycycline 100mg for 12 weeks.

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