Comparison of Efficacy of Conventional Nonmodified-Release Minocycline and Newer Extended-Release Minocycline in Treatment of Acne Vulgaris

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Abstract

Aims: The aim is to study the efficacy of conventional and extended-release minocycline therapy in acne vulgaris and to compare the two regimens for the efficacy and side effects. Materials and Methods: An open, randomized, comparative, prospective study was conducted on forty newly diagnosed cases of acne vulgaris (Grades 2 and 3) with more than 15 lesions. Patients were randomly allotted into one of the two groups which received extended-release minocycline and conventional minocycline, respectively, for 3 weeks. Both groups were prescribed local application of benzoyl peroxide 2.5% at night. All the patients were evaluated at the end of 3 weeks using paired and unpaired t-test. Results: Improvement was noted in patients belonging to both the groups. When both the groups were compared statistically using unpaired t-test, extended-release minocycline was significantly better in the treatment of inflammatory papules. Conclusions: Both conventional minocycline and extended-release minocycline were effective in the treatment of moderate and moderately severe acne vulgaris. Statistically inflammatory lesions respond better to extended-release minocycline.

Keywords: Acne vulgaris, conventional, extended release, minocycline

INTRODUCTION

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit that affects 85% of adolescents and young adults. It results from androgen-induced increased sebum production, altered keratinization, inflammation, and bacterial colonization of hair follicles by Propionibacterium acnes. It is the most common skin disease worldwide, characterized by noninflammatory, open or closed comedones and inflammatory papules, pustules, and nodules. It is seen more in females than males. If left untreated, severe acne can lead to disfigurement due to scarring.

Oral antibiotics continue to play an important role in the treatment of moderate-to-severe acne. Minocycline is a semisynthetic tetracycline antibiotic effective against a wide range of aerobic and anaerobic Gram-positive and Gram-negative bacteria. It is highly active in the pilosebaceous complex, due to its great lipophilicity, and therefore has been used in the treatment of moderate-to-severe papulopustular acne for a long time. Besides the antimicrobial activity, minocycline has an anti-inflammatory action, due to the reduction in neutrophilic chemotaxis, the inhibitory effect on pro-inflammatory cytokines, and the reduction in sebum-free fatty acids and bacterial lipases. In 2006, the Food and Drug Administration approved a new extended-release formulation of minocycline. This formulation allowed the reduction of some dose-related adverse events, such as those affecting the vestibular system. Apart from the dose-related events (nausea, vomiting, and dizziness), minocycline is also known to induce hyperpigmentation and is rarely responsible for autoimmune disorders, hypersensitivity reactions, and serum sickness-like reactions.

The latest guidelines in the treatment of acne recommend a dose of 50–100 mg once or twice a day for the nonmodified-release
minocycline and 1 mg/kg daily for the new extended-release formulation. This agent is most appropriately used in combination with a topical regimen containing benzoyl peroxide and/or retinoid.\(^6\)

The present open, randomized, comparative, prospective study was conducted to compare the efficacy of the conventional nonmodified-release minocycline with the newer extended-release minocycline in the treatment of acne vulgaris.

**Aim**

To compare the efficacy of conventional minocycline and extended-release minocycline in the treatment of acne vulgaris.

**Objectives**

1. To study the efficacy of conventional minocycline therapy in acne vulgaris
2. To study the efficacy of extended-release minocycline therapy in acne vulgaris
3. To compare the above two regimens for the efficacy and side effects.

**Materials and Methods**

This study was done in a tertiary care hospital. 40 newly diagnosed cases of acne vulgaris (Grades 2 and 3 based on grading system of Indian authors\(^7\)) with more than 15 lesions and belonging to the age group of 18–26 years were included in the study and randomly allotted into one of the two groups which received extended-release minocycline and conventional minocycline, respectively, for a period of 3 weeks. Both groups were prescribed local application of benzoyl peroxide 2.5% at night. A detailed history was taken which included the onset, duration and progress of condition, history of similar complaints, and history of any other underlying illness. Patients with polycystic ovarian disease, drug-induced acne, contraindications to oral minocycline, and those already on treatment were excluded from the study. Patients were advised to stop the use of medicated cosmetics in the entire study duration. A detailed clinical examination was done which included counting the acne lesions on the face on day 0 and day 21, by dividing the face into four quadrants. The lesions were divided into noninflammatory papules which included open, closed comedones and skin-colored papules; and inflammatory papules and pustules. After taking the patient’s written informed consent, photographic evidence was also taken on the same days. The percentage of reduction in the lesional count at the end of 21 days was considered as primary endpoint measurement. It was an open study. Paired \(t\)-test was used to calculate \(P\) value in each group (intragroup), whereas unpaired \(t\)-test was used to calculate \(P\) value while comparing the two groups (intergroup).

**Results**

A total of 40 newly diagnosed patients, 13 males and 27 females with acne Grades 2 and 3, were included in the study. 20 patients were started on conventional minocycline while the remaining 20 were started on extended-release minocycline. There were 6 males and 14 females in the conventional minocycline group and 7 males and 13 females in extended-release minocycline group. The mean age was 21.3 years in conventional minocycline group and was 21.2 years in extended-release minocycline group.

Improvement was noted in patients belonging to both the groups [Figures 1 and 2, Tables 1 and 2]. After applying paired \(t\)-test, it was found that \(P < 0.05\). Hence, reduction of lesions was statistically significant in both the treatment groups.

When both the groups were compared statistically using unpaired \(t\)-test, extended-release minocycline was significantly better in the treatment of inflammatory papules. However, there was no significant difference in the other type of lesions [Table 3].

**Discussion**

Tetracyclines are bacteriostatic antibiotics and are considered broad spectrum because they are active against a wide range

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**Table 1: Reduction in lesional count with conventional minocycline (paired \(t\)-test)**

|                       | Noninflammatory papules | Inflammatory papules | Pustules |
|-----------------------|-------------------------|----------------------|---------|
| Percentage reduction  | 45.73                   | 45.42                | 78.69   |
| Significant (two-tailed) | 0.000                  | 0.000                | 0.001   |
| \(P\)                 | <0.05                   | <0.05                | <0.05   |

**Table 2: Reduction in lesional count with extended-release minocycline (paired \(t\)-test)**

|                       | Noninflammatory papules | Inflammatory papules | Pustules |
|-----------------------|-------------------------|----------------------|---------|
| Percentage reduction  | 45.30                   | 65.48                | 87.54   |
| Significant (two-tailed) | 0.000                  | 0.001                | 0.000   |
| \(P\)                 | <0.05                   | <0.05                | <0.05   |
of aerobic and anaerobic Gram-positive and Gram-negative bacteria. Minocycline, a semisynthetic, second-generation tetracycline, acts by inhibiting protein synthesis by binding to 50S ribosomal subunit and preventing translocation. Minocycline being lipophilic achieves greater tissue concentration and is thought to be more effective than doxycycline in acne, a view held by the Global Alliance. It can be taken more conveniently as once or twice daily dose compared with the generally more frequent dosing of other tetracyclines.

The most common known side effects of minocycline are nausea, vertigo, and mild dizziness. Some systemic side effects such as gastrointestinal disturbances, tooth discoloration, enamel hypoplasia, autoimmune hepatitis, and drug hypersensitivity syndrome may occur. Cutaneous brown-black hyperpigmentation may be diffuse (muddy skin syndrome) or varying patterns involving the photo-exposed areas and periorbital area or lesional pigmentation including scars.

Minocycline has been studied and tested individually for treating acne, and it has also been compared with azithromycin for the treatment of acne. It has been found to be a good and effective choice of antibiotic for acne. Knowing that extended-release minocycline has a lot of advantages over conventional-release minocycline such as lesser frequency of administration leading to better compliance, lesser dose-related side effects; it was imperative to study whether it is superior to conventional minocycline in the treatment of acne. Benzoyl peroxide has been an important component of topical therapy for acne vulgaris for more than five decades due to its ability to markedly reduce *P. acnes* and inflammatory acne lesions and its ability to moderately reduce noninflammatory acne lesions. It is directly toxic to bacteria. It does not alter bacterial structure, specific enzymes, and/or nuclear and cytoplasmic proteins, unlike other antibiotics. As a result, benzoyl peroxide has not been associated with the development of *P. acnes* resistance. The addition of benzoyl peroxide to antibiotic therapy reduces the risk of bacterial resistance. Therefore, both the groups were given topical benzoyl peroxide 2.5% gel.

It was observed that in 3 weeks, all patients showed statistically significant reduction in their acne lesions. Therefore, it can be deduced that both these forms of minocycline are effective for treating acne. However, extended-release minocycline is better than conventional minocycline in the treatment of inflammatory papules. It is equally efficacious to conventional minocycline when compared for other types of acne lesions. Reduced frequency of medication is a major advantage with extended-release minocycline.

Limitations of the study are lack of blinding and short duration of the treatment and follow-up. The duration of treatment should have been longer, that is, 6 weeks. However, to ensure proper follow-up and avoid dropouts, the duration of the study was fixed to 3 weeks. Assessment of hypersensitivity for both forms of minocycline is required to conclusively determine the better form of regimen. Limited sample size which may skew the data is another limitation. However, a larger multicentric randomized trial is advocated based on the results of this study.

### Conclusions

Both conventional minocycline and extended-release minocycline were effective in the treatment of moderate and moderately severe acne vulgaris. Although statistically not significant, pustular lesions respond better to extended-release minocycline whereas noninflammatory lesions decrease more with conventional minocycline. Statistically inflammatory lesions respond better to extended-release minocycline.

Given the advantage of reduced frequency of medication, extended-release minocycline could be preferred as the better option among the two for treatment of acne.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names

### Table 3: Conventional minocycline versus extended-release minocycline: Reduction in lesional count

|                        | Percentage reduction in noninflammatory papules | Percentage reduction in inflammatory papules | Percentage reduction in pustules |
|------------------------|-----------------------------------------------|--------------------------------------------|---------------------------------|
| Conventional minocycline | 45.73                                         | 45.42                                      | 78.69                           |
| Extended-release minocycline | 45.30                                         | 65.48                                      | 87.54                           |
| Significant            | 0.780                                         | 0.027                                      | 0.635                           |
| \( P \)                | <0.05                                         | <0.05                                      | <0.05                           |

**Figure 2:** Conventional minocycline – before and after treatment
and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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