Introduction

Acne vulgaris is a chronic inflammatory disease of pilosebaceous units characterized by comedones, papules, pustules, nodules, cysts, abscesses, and later on sometimes as widespread scarring. This disease occurs worldwide and usually starts in adolescence and resolves by mid-twenties. It is the most common skin disorder, and different studies have shown prevalence rates ranging from 28.9% to 91.3% in adolescents. The primary and the pathognomonic lesion in acne is microcomedo, a microscopic lesion invisible to the eye. Some of these evolve into noninflammatory comedo or inflammatory lesions such as papule, pustule, or nodule. According to the severity of acne, there are various modalities of treatment, and they include both systemic and topical therapy. New modalities of treatment have been designed due to the better understanding of the pathogenesis. The most guidelines recommend oral antibiotics as the primary indication for moderate-to-severe inflammatory acne. Tetracycline and macrolide group of antibiotics have been in use for long. However, increasing Propionibacterium acnes resistance has resulted in unresponsiveness. Use of oral retinoids, isotretinoin has revolutionized acne treatment but is associated with many adverse effects such as dryness of lips, serum lipid derangement, hepatotoxicity, benign intracranial hypertension, teratogenicity, psychiatric effects, and musculoskeletal complaints especially in young adults.

There are very few reports regarding the effectiveness of levofloxacin in the treatment of inflammatory acne vulgaris. Once-daily 500 mg levofloxacin has been used for folliculitis, furunculosis, cellulitis, etc., It is bactericidal against Propionibacterium acnes. This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

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and acts by inhibition of DNA gyrase. The pharmacokinetic and pharmacodynamic profiles of fluoroquinolone feature the high bioavailability, long serum half-lives, allowing once-daily dosing, and less adverse effects. The studies concluded that once-daily 500 mg LVFX was well tolerated and may prove useful as a new drug for the treatment of acne because of its high tissue accumulation and remarkable efficacy. LVFX in these studies achieved marked reduction of acne papules and without significant side effects. No strain of P. acne resistant to levofloxacin was found in the study. We decided to use levofloxacin in inflammatory acne and to compare it with minocycline for inflammatory acne.

**Methods**

A study was conducted during January 2015–June 2015 to assess the efficacy of two treatment regimens in the patients with moderate-to-severe acne vulgaris: oral levofloxacin and oral minocycline, after institutional ethical committee approval. The study comprised 60 untreated cases of acne vulgaris of Grade 2 and 3 attending the outpatient department of dermatology at tertiary care hospital. A total of 60 patients allotted randomly in two groups of 30 each. Convenient sample size of 30 was selected. The patients with age <12 years, chronic kidney and liver disease, active tuberculosis, chronic alcoholism, immunocompromised patients, pregnant and lactating mothers, and those who have received systemic anti-acne treatment in the past 3 months were excluded from the study. The appropriate washout period was given for other topical and systemic medications used for acne. The evaluation was done by a blinded investigator.

A special pro forma was prepared, and the age, sex, occupation of the patient, and other data were recorded. A detailed history was noted with a particular reference to the onset, duration and evolution of acne, the role of predisposing factors including genetic and seasonal factors, and details of medications previously used. Before starting treatment, all patients were thoroughly explained about study protocol, and written informed consent was obtained. Blood investigation, such as complete blood count, hemoglobin, liver and kidney function test, sonography abdomen, and enzyme-linked immunosorbent assay for human immunodeficiency virus, was performed at 1st visit. X-ray chest and Mantoux test were performed to rule out tuberculosis. Baseline photographs were taken. Levofloxacin was given at dose of 500 mg/day for 30 days along with topical benzoyl peroxide 2.5% gel. Results were assessed at 2, 4, 8, and 12 weeks according to the global acne grading system (GAGS) [Table 1].

Moreover, another group received minocycline 100 mg for 3 months along with topical benzoyl peroxide, and they were advised to take sun protection. Results were assessed at 2, 4, 8, and 12 weeks after starting treatment according to the GAGS. In our study, all the participants and outcome assessor were blinded.

**Results**

A total of 60 patients of acne vulgaris coming to the outpatient department of tertiary care hospital were included in the study [Figure 1]. A total of 56 patients completed the study, and four patients were lost to follow-up (two from levofloxacin group and two from minocycline group). Out of the 60 patients, 38 were female and 22 were male. There were 10 males and 20 females in levofloxacin group and 12 males and 18 females in minocycline group. Mean age in levofloxacin group was 25 and in minocycline group was 27 [Table 2]. The majority of the patients were of Fitzpatrick skin type 4 and 5.

At 0 week, 13 patients (43.33%) had moderate acne, 17 patients (56.66%) had severe acne in levofloxacin group, whereas in minocycline group, 18 patients (60%) had moderate acne and 12 patients (40%) had severe acne [Table 3 and Figure 2].

At 4 weeks, in levofloxacin group, a number of patients with mild acne were 16 (53.33%), moderate acne were 10 (33.33%), and severe acne were 2 (6.66%). In minocycline group,
eight patients (26.6%) had mild acne, 19 patients (63.3%) had moderate acne, and severe in 1 patient (3.3%). Thus, comparing the mean of both the groups, we can conclude that levofloxacin is a better drug as compared to minocycline at the end of 4 weeks \((P = 0.05)\) [Table 4 and Figures 3,6-9]. At 12 weeks, in levofloxacin group, a number of patients with mild acne were 5 (16.6%), moderate acne were 22 (73.3%), and severe acne was 1 (3.3%). In minocycline group, 23 patients (76.6%) had mild acne, 6 patients (16.6%) had moderate acne, and none had severe acne. Thus, comparing the mean acne score, i.e., 22.89 (levofloxacin) and 14.39 (minocycline), we can conclude that minocycline is a better drug at the end of 12 weeks \((P < 0.001)\) [Table 5 and Figures 4,10-13].

As depicted in the graph, according to the GAGS, there was a significant decrease in score in levofloxacin group as compared to minocycline group. \((P = 0.05)\) at 4 weeks [Figure 1 and 2]. At 8 weeks and 12 weeks, decrease in score was more in minocycline group \((P < 0.024)\) and \((P < 0.001)\), respectively calculated by applying unpaired \(t\)-test [Table 6 and Figures 3-5].

According to the percentage of decrease in inflammatory count from baseline, there was a decrease in inflammatory lesion count by 58% at 4 weeks which increased to 81.1% at the end of 12 weeks in levofloxacin group. In minocycline group, a decrease in inflammatory lesion count at 4 weeks was 36.6% and 12 weeks was 68%.

**DISCUSSION**

We conducted a trial of oral levofloxacin in inflammatory acne vulgaris and compared it with oral minocycline. We included 30 patients in each group, and both groups were comparable at baseline. Mean age was 25 in levofloxacin

### Table 3: Baseline global acne grading score in both groups

| Severity score | Levofloxacin (%) | Minocycline (%) | Statistics (\(t\)-test) |
|----------------|-----------------|-----------------|------------------------|
| 1-18 (mild)    | 0               | 0               | \(P\) value not significant |
| 19-30 (moderate)| 13 (43.33)     | 18 (60)         |                        |
| 31-38 (severe) | 17 (56.66)     | 12 (40)         |                        |
| >39 (very severe) | 0              | 0               |                        |
| Average        | 31.32           | 30.11           |                        |

### Table 4: At 4 weeks, global acne grading system in both group

| Severity score | Levofloxacin (%) | Minocycline (%) | Statistics (\(t\)-test) |
|----------------|-----------------|-----------------|------------------------|
| 1-18           | 16 (53.33)      | 8 (26.6)        | \(P=0.05\) (significant) |
| 19-30          | 10 (33.33)      | 19 (63.3)       |                        |
| 31-38          | 2 (6.66)        | 1 (3.33)        |                        |
| >39            | 0               | 0               |                        |
| Average        | 18.71           | 20.96           |                        |

### Table 5: At 12 weeks, global acne grading in both the groups

| Severity score | Levofloxacin (%) | Minocycline (%) | Statistics (\(t\)-test) |
|----------------|-----------------|-----------------|------------------------|
| 1-18           | 5 (16.6)        | 23 (76.6)       | \(P<0.001\) (highly significant) |
| 19-30          | 22 (73.33)      | 5 (16.6)        |                        |
| 31-38          | 1 (3.3)         | 0               |                        |
| >39            | 0               | 0               |                        |
| Average        | 22.89           | 14.39           |                        |
group, whereas it was 27 in minocycline group. At the end of 4 weeks, after administering 500 mg of levofloxacin and 100 mg of minocycline daily, according to the GAGS, there was a significant decrease in acne score in levofloxacin group as compared to minocycline group. However, at 8 and 12 weeks, decrease in the score was more in minocycline group. Hence, a decrease in inflammatory lesion count was faster with levofloxacin (58%) within 4 weeks as compared to minocycline (36.6%), but it had increased subsequently. However, in minocycline group, the score further decreased after 4 weeks. Hence, prolonged treatment with minocycline proved satisfactory as compared to the short course of levofloxacin (4 weeks).

Kawada et al. in 2002[8] administered levofloxacin 100 mg three times a day for 4 weeks to 35 patients, 25 females and 15 males, whereas we gave 500 mg levofloxacin daily for 4 weeks in 30 patients, 20 females and 10 males. The mean age was 24 years in their study and 25 years in our study. No patient discontinued study because of adverse events, whereas two patients discontinued in our study because of gastrointestinal adverse effects, i.e., nausea, vomiting. They found that a decrease in the inflammatory count was 62.9% which was comparable to ours, i.e., 58% at 4 weeks. Uchida in 2011[9] administered 500 mg once-daily levofloxacin for 2 weeks, whereas we gave 500 mg levofloxacin for 4 weeks. A total of 19 patients, 15 females and four males were included in their study, whereas 20 females and 10 males were present in this study. Mean age of the patients was 21.9 years while 25 in our study. No patient discontinued their study because of adverse events. They found that decrease in inflammatory count (papules and pustules) was 62.2% at 2 weeks which was comparable to ours, i.e., 58% at 4 weeks.

We found similar response on administering oral minocycline as compared to studies in the literature carried

Table 6: Comparison of mean score in both the group and statistics

| Week  | Levofloxacin mean score | Minocycline mean score | Statistics (*t*-test) |
|-------|------------------------|-----------------------|----------------------|
| 0 week| 31.32                  | 30.11                 | *P* value (not significant) |
| 4 weeks| 18.71                  | 20.96                 | *P* =0.05 (significant)   |
| 8 weeks| 20.68                  | 17.96                 | *P* =0.024 (significant)   |
| 12 weeks| 22.89                 | 14.39                 | *P* <0.001 (highly significant) |

**Figure 5:** Comparison of the mean score in both the groups

**Figure 6:** Baseline photograph (Minocycline group)

**Figure 7:** Photograph at 4 weeks (Minocycline group)

**Figure 8:** Baseline photograph (Levofloxacin group)
out by Dreno et al.,[11] Grosshans et al.,[12] and Stewart et al.[13] at 3 months.

Dreno et al.[11] on administering oral minocycline 100 mg once-daily found a decrease in inflammatory lesion count to be 63.45% at the end of 12 weeks. It is comparable to our result, i.e., 58% decrease in inflammatory lesion count at 4 weeks after administering oral levofloxacin, but it had further increased to 81.1%. Thus, results of oral levofloxacin at 4 weeks are comparable with oral minocycline at the end of 12 weeks. Thus, levofloxacin is a faster-acting drug. Grosshans et al.[12] found a decrease in inflammatory lesion count to be 52.2% at the end of 12 weeks, while we found 58% decrease in inflammatory count at 4 weeks after administering oral levofloxacin, but it had increased to 81.1% at 12 weeks. Thus, the results of oral levofloxacin are better at 4 weeks, and it is a faster-acting drug.

Stewart et al.[13] on administering minocycline found that the decrease in inflammatory lesion count at the end of 12 weeks to be 50% which is comparable to our finding in levofloxacin group, i.e., 58% at 4 weeks. Thus, oral levofloxacin gives better results at the end of 4 weeks.

The first line of treatment for inflammatory acne is antibiotic, however, taking into consideration of increasing propionibacterium resistance to tetracycline group of drugs and macrolides, levofloxacin is a better option for initial treatment of inflammatory acne. As isotretinoin which cannot be combined with tetracyclines because of increased risk of pseudotumor cerebri and macrolides becoming resistant day-by-day, levofloxacin is a better option to be combined with isotretinoin for faster and better control of inflammatory acne. Considering levofloxacin as an important second-line drug for tuberculosis, it was only given for 4 weeks.

We found thus levofloxacin is responsible for rapid control of inflammatory acne; however, sudden withdrawal leads to exacerbation of the disease. Thus, levofloxacin should be combined with drug, such as isotretinoin, from starting or after an initial decrease in inflammatory lesion count for long-term remission. Our study concludes that levofloxacin is a better drug to decrease initial inflammatory acne as compared to minocycline.
Our study has some limitations. Benzoyl peroxide was combined with oral antibiotics in both the groups thereby confounding their effects. As the duration of levofloxacin therapy was 1 month and that of minocycline was 3 months, double blinding was difficult. We recommend furthermore double-blind, randomized controlled studies of a greater sample size to evaluate further safety and effectiveness of oral levofloxacin and minocycline in inflammatory acne.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names 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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