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# Comparison of Efficacy and safety of topical 1% Nadifloxacin and Tretinoin 0.025% versus 1% clindamycin and Tretinoin 0.025% in patients of mild-to-moderate acne vulgaris

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## Abstract

***Background:*** *Acne vulgaris causes cosmetic impairment and psychological destabilization. User-friendly combination anti-acne therapy has synergistic and additive actions on multi-pathogenetic factors, thus enhancing therapeutic efficacy and minimizing adverse effects. The current study was aimed to analyze the efficacy and safety of topical 1% Nadifloxacin and Tretinoin 0.025% versus 1% clindamycin and Tretinoin 0.025% in patients of mild-to-moderate acne vulgaris.* ***Methods****: This cross-sectional study was conducted in Prathima Institute of Medical Sciences, Naganoor, Karimnagar. The mild to moderate acne vulgaris patients were randomly allotted to two groups. Group I (Nadifloxacin + 0.025% tretinoin) and group II (1% clindamycin + 0.025% tretinoin). The application on the face once daily evening was left overnight and the efficacy was assessed by comparing the mean reduction in inflammatory and non-inflammatory areas after 12 weeks of application.* ***Results****: A total of 100 patients participated in this study out of which 70% were females and 30% were males. Based on the grading of acne mild acne was seen in 42% of cases and moderate acne was seen in 58% of cases. The mean duration of the disease in all cases was 55.61 ± 12.5 days. The mean reduction was found to be greater in group I as compared to that in group II and the mean difference between both the groups was found to be statistically significant (p-value < 0.05).* ***Conclusion:*** *The current study, found that the overall performance of 1% Nadifloxacin and Tretinoin 0.025% is more efficacious than 1% clindamycin and Tretinoin 0.025% in patients with mild-to-moderate acne vulgaris. Both the combinations appear to be safe as far as the adverse reactions are concerned.*

***Keywords:*** *Nadifloxacin, Fluoroquinolones, Clindamycin, Tretinoin*

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## Introduction

Acne vulgaris is a self-limited, chronic inflammatory disease of the pilosebaceous unit. [1, 2] The condition usually starts in adolescence and frequently resolves by the mid-twenties. However, in 7–17% of individuals, clinical acne persists beyond the age of 25 years. It has been found that acne affects nearly 80% of individuals between puberty and 30 years of age. In India, prevalence data have reported that acne is present in 50.6% of boys and 38.13% of girls in the age group 12-17 years. [3] Acne is multifactorial, and it is the sum of the various predisposing factors operating on susceptible individuals that determine the severity of the disease. Certain etiological factors that may precipitate acne include heredity, diet, menstruation, hormonal factors (like oral contraceptives), drugs like corticosteroids, androgens, corticotropins, iodides, bromides, lithium, etc., exposure to heavy oils, greases and tars, trauma or rubbing from tight clothes,

emotional stress, unfavorable climate, certain cosmetics. [4] The multi-pathogenetic mechanisms that acne vulgaris is usually attributed to are follicular epidermal hyperproliferation, excess sebum production, inflammation, and proliferation of resident microflora like *Propionibacterium acnes, Propionibacterium granulosum, Pityrosporum ovale, Staphylococcus epidermidis*. [1] The characteristic lesions of acne vulgaris are open and closed comedones, erythematous papules and pustules and in more severe cases nodules, deep pustules, pseudocysts, and possibly scarring. [5, 6] Antimicrobials, like Nadifloxacin and Clindamycin, are anti-inflammatory and mildly comedolytic. Nadifloxacin, a newer fluoroquinolone, inhibits the enzyme DNA gyrase that is involved in bacterial DNA synthesis and replication, thus inhibiting bacterial multiplication. Nadifloxacin inhibits the enzyme DNA gyrase, which is involved in bacterial DNA synthesis and replication, thus inhibiting the multiplication. Nadifloxacin also inhibits the enzyme DNA topoisomerase IV, which enhances its antibacterial spectrum to gram-positive, gram-negative as well as anaerobic bacteria such as Propionibacterium acnes as well as against methicillin-susceptible Staphylococcus aureus (MSSA) and Staphylococcus epidermidis, among others. Clindamycin, a lincosamide, inhibits protein synthesis by interfering with the formation of initiation complexes and with aminoacyl translocation reactions. [7] Clindamycin binds exclusively to the 50S subunit of bacterial ribosomes and suppresses protein synthesis by binding to the 50S ribosomal subunit. Retinoids, like tretinoin, are comedolytic and anti-inflammatory. Tretinoin has a selective affinity for retinoid receptors, like retinoic acid receptor α, retinoic acid receptor β, and retinoic acid receptor γ. [8] It stabilizes lysosomes, increases ribonucleic acid polymerase activity, increases prostaglandin E2, cAMP, and cGMP levels, and increases the incorporation of thymidine into DNA. Its action in acne has been attributed to decreased cohesion between epidermal cells and increased epidermal cell turnover. [8] This is thought to result in the expulsion of open comedones and the transformation of closed comedones into open ones. With this background, this study aimed to analyze the efficacy and safety of topical 1% Nadifloxacin and Tretinoin 0.025% versus 1% clindamycin and Tretinoin 0.025% in patients of mild-to-moderate acne vulgaris.

## Materials and Methods

This study was conducted in the Department of Dermatology, OPD in Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the participants of the study.

*Inclusion criteria*

1. Patients aged between 15-30 years
2. Males and females.
3. Patients with mild to moderate acne (grade – I & II)
4. Voluntarily willing to participate in the study

*Exclusion criteria*

1. Severe acne vulgaris
2. Drug-induced acne
3. Acne lesions on the trunk
4. Pregnant females
5. Immunocompromised patients and chronic medical illnesses

Based on the inclusion and exclusion criteria a total of n=100 cases were included in the study they were randomly allotted by computer-generated random number to two groups. **Group I** (Nadifloxacin + 0.025% tretinoin) and group II (1% clindamycin + 0.025% tretinoin). A detailed history was obtained with the proforma, giving special attention to the predisposition to acne. At the first visit, the patients were interviewed for their demographic profile, present, and history, personal history, medication history**,** etc. A systemic examination was performed. Then, the dermatologic evaluations were made. Each patient was examined for the baseline non-inflammatory, inflammatory, and total lesions counting and documented in their respective case record forms. Each patient was also assessed for the baseline acne severity grading as per the Investigators Global Severity Assessment (IGA) Scale. [9] Before the application of the topical anti-acne agents, the patients were advised to wash their face with clean water and dry it well.

The patients allotted in either group were prescribed to apply 1 fingertip unit (approximately 0.5 gram) of each study drug, at night, over the forehead, cheeks, chin, and nose, with a thin film evenly spread over the entire face. Special precaution was taken to avoid the periorbital, para nasal, and perioral areas. According to the prescription, the patients, allotted in either group, applied 0.025% tretinoin first. After half an hour, the group A patients applied 1% clindamycin over that, without washing the face and the group B patients applied 1% nadifloxacin over that, without washing the face. The respective medications were then left overnight. The following efficacy parameters are assessed, Number of non-inflammatory lesions (open and closed comedones) Number of inflammatory lesions (papules, pustules, nodules. The number of total lesions. At the baseline, the total number of lesions on the face was taken as 100%. Any reduction in the number of acne lesions, at follow-up, as compared with the
baseline was expressed as the percentage of improvement and graded. Evaluation for tolerability and safety parameters: They were also asked for the skin tolerability of the medications and the consequent side effects were observed during therapy. Dryness, Erythema, Burning, Peeling, and Irritation. Each parameter was assessed and graded at 2-, 4-, 8- and 12-weeks follow-up, by the Local Irritation Scale. 120 Each patient was evaluated on a scale from 0 (none), 1 (mild), 2 (moderate), and 3 (severe) at each visit. The final efficacy of the medications was evaluated at the end of 12 weeks and statistically analyzed. All the available data was uploaded on the MS Excel spreadsheet and analyzed by SPSS version 19 on windows format for descriptive statistics and Inferential statistics used were ANOVA for repeated measures and by Chi-Square Test.

## Results

Out of the n=100 cases studied 48% were between the age group 15 – 20 years and 30% were between the age group 21 – 25 years and 22% were between the age group 26 – 30 years the mean age of study patients was 19.5 years. Out of all the cases in this study, 70% were females and 30% were males. Based on the grading of acne mild acne was seen in 42% of cases and moderate acne was seen in 58% of cases. the mean duration of the disease in all cases was 55.61 ± 12.5 days.

**Table 1:** Demographic profile of patients included in the study

| *Demographic characteristics* | *Group A* | *Group B* |
|---|---|---|
| No. of cases | 50 | 50 |
| Gender | | |
| Male | 12 | 18 |
| Female | 38 | 32 |
| Grade of acne | | |
| Mild | 25 | 17 |
| Moderate | 28 | 30 |
| Mean age (years) ± SD | 18.5±2.5 | 19.0 ± 1.5 |

After a comparison of percentage reduction in non-inflammatory lesions of the two groups, it was found that there was a greater reduction in group I than in group II. The mean reduction was increased based on the duration of the application and the maximum values were found at the end of 12 weeks of application depicted in table 2.

**Table 2:** Depicting the reduction of the non-inflammatory lesion at different intervals

| Non-inflammatory lesions | Reduction from baseline | Week 2 | Week 4 | Week 8 | Week 12 |
|---|---|---|---|---|---|
| Group I | Mean reduction | 4.5 ±1.2 | 15.1± 1.7 | 23.6 ± 3.5 | 28.8± 5.1 |
| | % Reduction | 7.9 | 30.2 | 44.99 | 58.9 |
| Group II | Mean reduction | 3.9 ±1.5 | 7.4 ± 2.8 | 13.75 ± 2.3 | 25.2 ± 5.0 |
| | % Reduction | 7.0 | 14.9 | 25.8 | 46.8 |

The reduction of inflammatory lesions was compared between two groups at different intervals of times. The percentage of reduction in group I reached 51.5% at the end of 12 weeks

and a similar point in group II the reduction values were 35.63% depicted in table 3.

**Table 3:** The reduction of Inflammatory lesions at different intervals

| Inflammatory lesions | Reduction from baseline | Week 2 | Week 4 | Week 8 | Week 12 |
|---|---|---|---|---|---|
| Group I | Mean reduction | 2.9 ± 1.5 | 8.7 ± 1.77 | 11.5 ± 1.33 | 13.1 ± 3.21 |
| | % Reduction | 11.5 | 34.8 | 45.6 | 51.5 |
| Group II | Mean reduction | 2.4 ± 0.9 | 6.5 ± 1.2 | 7.66 ± 1.89 | 10.8 ± 2.1 |
| | % Reduction | 8.9 | 23.4 | 26.7 | 35.63 |

The mean reduction in non-inflammatory lesions was 29.5 ± 4.2 in group I and 25.2 ± 2.3 in group II therefore the mean reduction was significantly higher in group I as compared to group II. The mean reduction in inflammatory lesions was 13.2 ± 2.5 in group I and 10.5 ± 2.7 in group II and the overall reduction was found to be greater in group I as compared to that in group II and the difference was found to be significantly depicted in table 4.

**Table 4:** comparison of reduction of Inflammatory lesions in two groups

| Lesions | Group I | Group II | Mean difference | t value | p-value |
|---|---|---|---|---|---|
| Non-inflammatory lesions | 29.5 ± 4.2 | 25.2 ± 2.3 | 4.3 | 3.69 | 0.012* |
| Inflammatory lesions | 13.2 ± 2.5 | 10.5 ± 2.7 | 2.7 | 2.15 | 0.0413* |

* Significant

In this study, after 12 weeks of therapy, in group I 80% of the patients achieved significant clinical improvement as the global severity scale of assessment was classified as clear or almost clear. In group II 62% of patients were able to achieve such results at the end of 12 weeks. The difference was found to be statistically significant, after applying the Chi-square test. In this study, only 3(6%) patients in group I and 5(10%) patients in group B were observed to develop very mild erythema. There was no statistically significant difference in the observations between the two groups of patients. Topical Nadifloxacin 1% in combination therapy with tretinoin 0.025% was as well tolerated as topical clindamycin 1% in combination therapy with tretinoin 0.025%.

## Discussion

Topical preparations constitute the sole treatment in many patients with acne vulgaris and are a part of the therapeutic regimen in almost all patients. Topical monotherapies can address almost all the causes of acne. However, no topical medicine can suppress excess sebum production. Topicals, including retinoids (tretinoin, isotretinoin, adapalene, tazarotene) and anti-microbials (nadifloxacin and clindamycin) act as keratolytic that have previously been reserved for non-inflammatory lesions. Antibacterial agents reduce the number of *P. acnes* and can also work as weak comedolytics and anti-inflammatory agents. Long-term use of topical antibacterials causes resistant forms of *P. acnes* and therefore is not recommended for chronic maintenance of acne. [10] Topical antibiotics reduce the population of *P. acnes* on the skin, particularly within follicles, and decrease the levels of the pro-inflammatory products of *P. acne*. [11] A total of 100 patients participated in this study out of which 70% were females and 30% were males. Based on the grading of acne mild acne was seen in 42% of cases and moderate acne was seen in 58% of cases. the mean duration of the disease in all cases was 55.61 ± 12.5 days. The mean reduction was found to be greater in group I as compared to that in group II and the mean difference between both the groups was found to be statistically significant (p-value < 0.05). Thus, the mean reduction in non-inflammatory lesions, inflammatory lesions, and total lesions with nadifloxacin and tretinoin combination therapy was found to be greater as compared to that with clindamycin and tretinoin combination therapy and the mean difference between both the groups was found to be statistically highly significant in case of non-inflammatory lesions (p-value < 0.05), while the mean difference

between both the groups was found to be statistically significant in case of inflammatory and total lesions (p-value < 0.05). In this study, after 12 weeks of therapy, in group I, 80% of the patients showed improvement in acne lesions as per Investigators Global Severity Assessment Scale of acne whereas, in group II, 62% of the patients showed improvement in acne lesions. It was found that both combinations were affected in acne reduction as seen by the reduction in inflammatory lesions and non-inflammatory lesions. The benefit of the combination of antibiotics with retinoids could be due to thinning effect of retinoids on the stratum corneum and increased comedonal drainage and it also helps in penetration of antibiotics in deeper layers of skin. [12-14] In this study, only 3(6%) patients in group I and 5(10%) patients in group B were observed to develop very mild erythema. Therefore, the overall adverse reactions were mild and self-limiting, and they did not result in stopping the therapy.

## Conclusion

Within the limitations of the current study, it was found that the overall performance of 1% Nadifloxacin and Tretinoin 0.025% is more efficacious than 1% clindamycin and Tretinoin 0.025% in patients of mild-to-moderate acne vulgaris. Both the combinations appear to be safe as far as the adverse reactions are concerned.

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***Ethical Permission*: Obtained**

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