

# Comparison of efficacy and safety of topical 1% nadifloxacin and tretinoin 0.025% combination therapy with 1% clindamycin and tretinoin 0.025% combination therapy in patients of mild-to-moderate acne

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## Abstract

**Background:** Topical retinoids in combination with antimicrobials have been proven to reduce acne lesions faster and to a greater degree than antimicrobial therapy alone .

**Aims and Objectives:** To compare the efficacy and safety of topical combination of 1% Nadifloxacin [NAD] and 0.025% Tretinoin [Tr] with 1% Clindamycin [CLN] and 0.025% Tr in patients of mild to moderate acne vulgaris of the face.

**Material and Methods:** There were two groups (40 patients in each group): Group A received (NAD+Tr) combination therapy and group B received (CLN+Tr) combination therapy. Efficacy was assessed by any reduction in the mean number of inflammatory lesions(IL), non-inflammatory lesions(NIL) and/or total lesions(TL) as well as by using Evaluator's Global Severity Scale (EGSS) of acne and safety was assessed by adverse effects of study medications at 0, 6 and at 12 weeks follow-up.

**Results:** Both the study groups showed statistically significant intragroup reduction in NIL, IL and TL after 12 weeks of therapy. There was no statistically significant reduction at the end of 6 weeks of therapy in both the groups. At the end of 12 weeks of therapy there was a statistically significant reduction in IL, NIL and TL in group A. There was no statistically significant difference in the occurrence of adverse effects in both the groups.

**Conclusion:** Overall the study proved better efficacy of NAD+Tr compared to CLN+Tr. Medications of both the groups were safe and well tolerated.

**Keywords:** Acne vulgaris, retinoids, topical antimicrobials

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## INTRODUCTION

Acne vulgaris, a chronic inflammatory disease of the pilosebaceous units, is characterized by seborrhea,

formation of open and closed comedones, erythematous papules, pustules, and pseudocysts.<sup>[1]</sup> It is a common

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skin disorder affecting at least 85% of adolescents and young adults. The pathophysiology of acne vulgaris is complex. Initially, there is androgen-mediated stimulation of sebaceous gland activity followed by abnormal keratinization leading to follicular plugging (comedo formation). There is now proliferation of *Propionibacterium acnes* within the plugged follicle which is further worsened by inflammation. Topical retinoids such as tretinoin (Tr) are commonly prescribed along with combination of antibiotics such as clindamycin (CLN) and nadifloxacin (NAD) in treatment of mild-to-moderate acne vulgaris. This combination has proven to reduce acne lesions faster as it targets ductal hypercornification, *P. acnes* colonization, and inflammation and it also prevents development of antimicrobial resistance.<sup>[2]</sup> There are not many published studies till date that have evaluated the clinical effectiveness and safety of topical NAD + Tr compared to CLN + Tr (an accepted standard regimen) in mild-to-moderate facial acne. With this background, we undertook this prospective, randomized, parallel, open-label clinical trial in patients of mild-to-moderate acne vulgaris in our tertiary care hospital.

## MATERIALS AND METHODS

### Ethics

The study was approved by the Institutional Ethics Committee and written informed consent was obtained from all the participants before the conduct of the study. In case of patients aged below 18 years, assent was obtained along with written informed consent from parent(s)/legal guardian. The sanction from the Ethics Committee was obtained for the same.

### Selection of patients

The study was carried out on 80 patients (40 patients per group) from December 2013 to October 2014. Patients meeting the inclusion criteria were recruited from skin outdoor patient department of the institution.

### Inclusion criteria

1. Patients aged 12–25 years of either sex
2. Newly diagnosed (without prior history of acne) patients with mild-to-moderate acne on the face above the jawline (according to Evaluator's Global Severity Scale [EGSS]) were included in the study.<sup>[3]</sup>

### Exclusion criteria

1. Patients with severe and very severe grade acne vulgaris
2. Patients having other variants of acne: chloracne, oil acne, tropical acne, mechanical acne, and severe variants such as acne conglobata and acne fulminans
3. Patients having drug-induced acne
4. Pregnancy and lactating mothers

5. Patients with known hypersensitivity to any of the components of the drug were excluded from the study.

There were two groups, A and B:

- Group A: 1% NAD and Tr 0.025% topical combination therapy
- Group B: 1% CLN and Tr 0.025% topical combination therapy.

The patients were asked to follow up at the end of 6 weeks and 12 weeks of the treatment.

### Efficacy parameters

The efficacy was evaluated by inter- and intra-group reduction from baseline in the number of noninflammatory lesions (NIL) (comedones), inflammatory lesions (IL) [papules, pustules, and nodules], and in total number of acne lesions (TL). Intergroup improvement in acne as per EGCS was also evaluated.

Safety was evaluated by vigilant follow-up of patients for adverse drug reactions (ADRs) and recorded in case report form.

### Statistical analysis

After checking for normality of data using Kolmogorov–Smirnov test, intragroup mean reduction for IL, NIL, and TL was evaluated with the help of one-way ANOVA test. Intergroup comparison of two groups for IL, NIL, and TL was evaluated with the help of unpaired *t*-test. Categorical data were expressed using descriptive statistics as percentage of participants showing improvement as per EGSS for acne and comparison between two groups was done with the help of Chi-square test. Occurrence of ADRs was also compared by Chi-square test. All the tests were done at 5% level of significance. All statistical analysis was done using statistical software GraphPad Prism version 6 (Armonk, NY and Microsoft Excel 2013).

## RESULTS

A total number of 80 patients were included in our study, and 40 patients were randomly allocated to each group. One patient in NAD + Tr group was lost in follow-up and did not participate in the study after baseline visit. Hence, total 79 patients (40 in CLN + Tr group and 39 in NAD + Tr group) completed the 12-week study. The demographic profile and characteristics of both the groups were comparable at baseline ( $P > 0.05$ ).

### Efficacy evaluation

#### Intragroup efficacy evaluation

Both the groups showed statistically significant intragroup

reduction in NIL, IL, and TL after 12 weeks of therapy ( $P < 0.01$ ) [Tables 1 and 2].

### Intergroup efficacy evaluation

Between the two groups, there was a statistically significant reduction in the mean number of NIL, IL, and TL in NAD + Tr group than CLN + Tr group at the end of 12 weeks ( $P < 0.05$ ) [Table 3]. However, this difference in the reduction of mean number of acne lesions was not statistically significant ( $P > 0.05$ ) when the two groups were compared at the end of 6 weeks of therapy.

### Improvement as per Evaluator's Global Severity Scale for acne

After 12 weeks of therapy, 17.94% of patients in the NAD + Tr group improved as per EGSS of acne compared

**Table 1: Number of lesions in topical clindamycin + tretinoin-treated group (n=40)**

	Baseline	6 weeks	12 weeks	P
Noninflammatory lesions	18.7±3.52	8.85±2.26	4.17±1.93	<0.0001***
Inflammatory lesions	4.72±1.18	1.27±0.71	0.72±0.78	<0.0001***
Total lesions	23.42±3.98	10.12±2.60	4.9±2.13	<0.0001***

Data depicted as: Mean±SD. SD=Standard deviation, P-value < 0.05 is flagged with one star (\*), P-value < 0.01 is flagged with two stars (\*\*), P-value < 0.001 is flagged with three stars (\*\*\*)

**Table 2: Number of lesions in topical nadifloxacin + tretinoin-treated group (n=39)**

	Baseline	6 weeks	12 weeks	P
Noninflammatory lesions	18.25±4.07	7.46±1.55	1.12±0.80	<0.0001***
Inflammatory lesions	4.53±1.07	0.97±0.53	0.05±0.22	<0.0001***
Total lesions	22.79±3.66	8.43±1.60	1.17±0.88	<0.0001***

Data depicted as: Mean±SD. SD=Standard deviation, P-value < 0.05 is flagged with one star (\*), P-value < 0.01 is flagged with two stars (\*\*), P-value < 0.001 is flagged with three stars (\*\*\*)

**Table 3: Comparative reduction in number of noninflammatory, inflammatory, and total lesions between the two groups after 12 weeks of therapy**

Reduction from baseline after 12 weeks of therapy	CLN + Tr (n=40)	NAD + Tr (n=39)	P
Noninflammatory lesions	-14.52±2.26	-17.12±3.83	0.0004***
Inflammatory lesions	-4.0±1.03	-4.48±1.12	0.0484*
Total lesions	-18.52±2.81	-21.61±3.52	<0.0001***

Data depicted as: Mean reduction±SD. SD=Standard deviation, CLN + Tr=Clindamycin + tretinoin, NAD + Tr=Nadifloxacin + tretinoin, P-value < 0.05 is flagged with one star (\*), P-value < 0.01 is flagged with two stars (\*\*), P-value < 0.001 is flagged with three stars (\*\*\*)

**Table 4: Side effects of medications**

Side effects	Clindamycin plus tretinoin n (%)	Nadifloxacin plus tretinoin n (%)	P
Erythema	1 (2.5)	0	1.000
Dryness	5 (12.5)	4 (10)	1.000
Scaling	3 (7.5)	3 (7.5)	1.000
Burning	8 (20)	9 (22.5)	0.7895
Pruritus	13 (32.5)	10 (25)	0.6219

Data depicted as: n (percentage)

to 12.50% of patients in the CLN + Tr group, but there was no statistically significant difference between the two groups ( $P > 0.05$ ).

### Safety evaluation

There were no serious side effects reported in both the groups. There was no statistically significant difference between the two groups ( $P > 0.05$ ) [Table 4].

## DISCUSSION

Acne due to its complex pathophysiology demands a combination therapy.<sup>[4,5]</sup> According to recent acne therapy guidelines, antibiotics should not be used alone due to fear of resistance. Combination with a topical retinoid is highly recommended.<sup>[6]</sup> Among topical antibiotics that are available in India, erythromycin and CLN are most popular. Topical clarithromycin, azithromycin, and NAD are also available in India, but trials for their efficacy and safety are lacking. Hence, we undertook a study to determine and compare the safety and efficacy of NAD and CLN in combination with topical retinoid (Tr) therapy in patients of mild-to-moderate acne.

Both the combinations were effective in acne as seen by the reduction in the number of IL, NIL, and TL in both the study groups. This finding reinforces the beneficial effect of combination therapy of topical antimicrobial agents with the topical retinoids. The beneficial effect could be due to the thinning effect of retinoids on the stratum corneum, along with its property of comedonal drainage, which facilitates the penetration of antibiotics up to deeper layers of the skin.<sup>[7-9]</sup>

NAD and Tr combination therapy group showed greater reduction in acne lesions compared to CLN and Tr group. This could be due to the fact that NAD is reported to have potent action against *P. acnes*, *Staphylococcus epidermidis*, and methicillin-resistant *Staphylococcus aureus* (MRSA), with no cross-resistance<sup>[10-12]</sup> with any other antibiotic or with another fluoroquinolone whereas there is emerging resistance of *P. acnes* to CLN.<sup>[13]</sup> NAD also has an additional beneficial action on T-cells and keratinocytes.<sup>[14]</sup>

The medications of both the groups were well tolerated in our study, which was also illustrated by previous studies.<sup>[15]</sup> There were no serious adverse effects reported in our study.

## CONCLUSION

We found out that NAD 1% plus Tr 0.025% combination is more efficacious than CLN 1% plus Tr 0.025%

combination over 12-week period in the treatment of mild-to-moderate acne vulgaris of the face and both the combinations of medications are safe.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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