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Original Research Article

Safety and efficacy of nadifloxacin versus clindamycin observed in a tertiary care teaching hospital of Deccan Plateau

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ABSTRACT

Background: Acne vulgaris is characterised by excess sebum production and inflammatory reaction in sebaceous glands. As propionibacterium is involved in aggravation of acne, antimicrobials like nadifloxacin and clindamycin were found to be effective in treatment.

Aim: Comparison of nadifloxacin with clindamycin in terms of inflammatory and non-inflammatory lesion count and global improvement rating, when given in combination with benzoyl peroxide in patients in acne vulgaris

Materials and Methods : Nadifloxacin 1%, benzoyl peroxide 2.5% and clindamycin 1% were used as topical treatment option. Study cohort was randomly divided into two groups: Nadifloxacin group and Clindamycin group. All subjects who were included in the study were instructed to apply a thin layer of medication over acne lesions; benzoyl peroxide 2.5% gel once daily at bedtime and clindamycin 1% gel or Nadifloxacin 1% gel twice daily. Efficacy is analysed by comparing changes in total, inflammatory and non-inflammatory lesion counts. In addition, global improvement was rated by patients using a six-point scale (worsening, no improvement, slight improvement, moderate improvement, good improvement, clearance) at end of treatment.

Results: There is progressive decline in number of inflammatory and non-inflammatory lesions in both groups. Analysis of lesion counts not showed any significant difference in between two groups. In global improvement rating scale, more number of patients using nadifloxacin with benzoyl peroxide reported good improvement compared to patients using Clindamycin with benzoyl peroxide. No patient in any group reported worsening of lesions. None of patients in study groups reported clearance. Two adverse events were reported during study, they were, burning sensation and dryness. There was no significant difference in incidence of adverse events in both treatment groups.

Conclusion: Topical Nadifloxacin, a new fluoroquinolone is effective, tolerable and safe for mild or moderate facial acne. Its clinical effectiveness is equivalent to clindamycin when used as add-on therapy to benzoyl peroxide.

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1. Introduction

Acne vulgaris is a disease characterised by more sebum production and inflammatory reactions in sebaceous glands, presents with comedones, papules, pustules, cysts and nodules. It occurs commonly on face but can also arise

on neck, chest, back and upper arms,¹ though disease sometimes can be self-limiting, its effects can be lifelong and it also presents with other skin lesions that occur from manipulation of lesions, which include pitted scars, dark marks and keloids.²

Increased sebum secretion is main cause for development of acne lesions, since sebum serves as nutrient source for Gram-positive bacterium *Propionibacterium*acnes.³

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Prevalence of acne remains high and its psychological impact is more. Hence, there is more patient-driven demand for better and convenient acne therapies.⁴

There is more need for topical medications as acne vulgaris require long term treatment, these include topical retinoids and topical antibiotics in monotherapy or in combination.^{5,6}

Combination therapy is more effective than monotherapy as it targets three major areas of acne pathophysiology.⁷ P. acnes proliferation, inflammation and hyperkeratinisation.^{8,9} Nadifloxacin, a topical fluoroquinolone, acts by inhibiting negative super coiling of bacterial DNA, effective against aerobic Gram-negative, Gram-positive and anaerobic bacteria.^{10,11}

Previous studies done¹² on topical nadifloxacin in acne vulgaris showed significant reduction in erythema, pain and itching with low incidence of adverse events.^{13,14} Benzoyl peroxide, effective topical agent in acne vulgaris since many years is available in different topical formulations,^{15,16} its high efficacy is due to oxidizing and anti-inflammatory activities, but its main side effect is skin irritation and bleaching of clothes.^{17,18} Clindamycin is available in topical form in combination with or without addition of zinc.^{19,20} though it produces minor side effects, sometimes it can produce pseudo membranous colitis.²¹

Problem with topical antibiotics is development of bacterial resistance when used as mono-therapy.²² Combination therapies are given importance to reduce skin sensitization,²³ antibiotic resistance and to enhance treatment outcomes.^{23,24} Multimodal therapy targeting different pathological processes simultaneously leads to better outcome.²⁵ Many studies reported combination therapy plays a pivotal role in improving patient adherence.²⁶

There are less published clinical studies comparing combinations of antimicrobial agents like clindamycin and nadifloxacin in patients of acne vulgaris. Hence present study was undertaken to compare efficacy and safety of nadifloxacin with clindamycin in combination therapy with benzoyl peroxide.

2. Materials and Methods

This is observational, open labelled and comparative study done in patients who are attending dermatology outpatient in a tertiary care centre, in South India. Study is conducted for a period of 3 months from February 2022 to April 2022. Prior approval from Institutional ethics committee was taken. Total acne lesion count is recorded at 0, 6 and 12 weeks of therapy. Patients of age between 14 to 30 years and patients with greater than 2 but less than 30 total acne lesions in face are included in study. Patients of age less than 14 or more than 30 and with total acne lesions less than 2 or more than 30 are excluded from study.

Study was conducted in accordance with good clinical practice guidelines. Drugs given to study subjects were already well-established and were in common use. Nadifloxacin 1%, benzoyl peroxide 2.5% and clindamycin 1% were used as topical treatment option. Study groups were randomly divided into two groups: Nadifloxacin group (20 patients; received topical Nadifloxacin 1% gel twice daily and benzoyl peroxide 2.5% gel once daily and Clindamycin group (20 patients received Clindamycin 1% gel twice daily with Benzoyl peroxide 2.5% gel once daily). All subjects were instructed to apply a thin layer of medication over lesions and application should last for 4 hours.

Efficacy is analysed by comparing changes in total, inflammatory and non-inflammatory lesion counts and global improvement was rated by patients using six-point scale (worsening, no improvement, slight improvement, moderate improvement, good improvement and clearance) at end of treatment. Side effects were assessed for severity and duration. Data obtained is analysed by using Microsoft excel and presented in tables and percentages.

3. Results

Mean age of subjects in nadifloxacin group was 22 compared to 20 years in clindamycin group, 50 % were males in nadifloxacin group while 40% in clindamycin group. There were no significant differences in baseline demographic and disease characteristics in two groups. At baseline, at end of 6 and 12 weeks, no significant difference of total lesion count was noted between two groups.

Table 1: Showing comparison of total lesion count in between two groups

| Total lesion count | Nadifloxacin group | Clindamycin group |
|----------------------|--------------------|-------------------|
| Baseline (0 weeks) | 25+/- 6 | 24+/-4 |
| Follow up (6 weeks) | 15+/- 4 | 16+/-3 |
| Study end (12 weeks) | 10+/- 2 | 11+/-2 |

Table 2: Showing comparison of inflammatory and non-inflammatory lesion count

| Visit | Lesion count | Nadifloxacin group | Clindamycin group |
|---------------------|-----------------|--------------------|-------------------|
| Baseline (0weeks) | Inflammatory | 8+/-3 | 17+/-3 |
| | Noninflammatory | 6+/-4 | 18+/-2 |
| Follow up (6weeks) | Inflammatory | 5+/-2 | 10+/-4 |
| | Noninflammatory | 4+/-1 | 12+/-2 |
| Study end (12weeks) | Inflammatory | 2+/-2 | 8+/-2 |
| | Noninflammatory | 3+/-2 | 8+/-2 |

For both groups, progressive decline in number of inflammatory and non-inflammatory lesion counts was observed; analysis of lesion counts at first follow up and at study end did not show any significant difference between two groups. In global improvement rating scale, more number of patients using nadifloxacin with benzoyl peroxide reported good improvement compared to patients using Clindamycin with benzoyl peroxide. No patient in any group reported worsening of lesions or clearance.

Two adverse events were reported during study, they were, burning sensation and dryness. There was no significant difference in incidence of adverse events in both treatment groups. About 5% patients suffered with dryness and 5% patients had burning sensation. None of patients needed treatment modification for adverse events.

4. Discussion

Four factors which contribute to development of acne lesions are plugging of follicles by debris, inflammation in skin, increased production of sebum and presence of bacteria *Propionibacterium acnes*. There are several different types of acne lesions and each individual may have predominantly one form of acne or a combination of lesions present at one time. Most common and effective treatments are topical therapies. These include retinoids, benzyl peroxide or topical antibiotics and their combinations.

Results from this study demonstrate reduction in total lesion count and both inflammatory and non-inflammatory lesions of acne over 12 week treatment period with two topical therapies (clindamycin with benzoyl peroxide and nadifloxacin with benzoyl peroxide). No differences between two therapies were observed in total, inflammatory or non-inflammatory lesion counts.

Study done by Green L²⁷ shows clindamycin was better tolerated than adapalene when given with benzyl peroxide and study done by Kaur J^{28,29} showed that Clindamycin with Benzoyl peroxide is better in reduction of lesion count and safety profile is better with Nadifloxacin when given with Benzoyl peroxide and study done by Ozgen ZY³⁰ showed inflammatory lesions better reduced with Nadifloxacin. Jackson JM³¹ showed Clindamycin was better tolerated in reduction of acne lesion count.

This study provides us with evidence that combination therapy of nadifloxacin and benzoyl peroxide is effective, tolerable and safe in cases of mild to moderate acne and comparable to that of existing clindamycin-benzoyl peroxide regimens.

Study was done for 12 weeks. Topical antibiotics are generally recommended for 8 weeks²⁴ with limitation of maximum 12 weeks. Duration of this study was similar to studies done by Gollnick and Ghali.^{34,35}

In our study, males and females were almost equal, correlates with sex distribution of studies done by Michael and Takigawa.^{36,37}

Table 3: Showing previous studies focussing on topical combination therapy for management of acne

| Previous studies | Findings |
|--|--|
| Clindamycin with benzoyl peroxide gel versus adapalene with benzoyl peroxide gel in mild to moderate acne. ²⁷ | Clindamycin with Benzoyl peroxide gel better tolerated during first 2 weeks of treatment; comparable efficacy at 8 weeks |
| Clindamycin with benzoyl peroxide versus nadifloxacin with benzoyl peroxide in moderate to severe acne. ²⁸ | Clindamycin with Benzoyl peroxide is better in reduction of lesion count; safety profile is better with Nadifloxacin with Benzoyl peroxide |
| Clindamycin with benzoyl peroxide gel versus clindamycin preparation. ²⁹ | Clindamycin with Benzoyl peroxide gel is more effective |
| Nadifloxacin versus nadifloxacin with benzoyl peroxide in mild to moderate Acne. ³⁰ | Both regimens were effective, well-tolerated; inflammatory lesions better reduced in Nadifloxacin with Benzyl peroxide group |
| Benzoyl peroxide with clindamycin gel vs clindamycin with tretinoin gel in acne ³¹ | Clindamycin with Benzyl peroxide gel better than Clindamycin with Tretinoin |
| Benzyl peroxide with clindamycin versus benzyl peroxide with clindamycin. ³² | Comparative efficacy |
| Adapalene with benzyl peroxide in moderate to severe acne. ³³ | Safe and effective in the long-term management of acne patients |

Common side effects of these medications are dryness and irritation of skin, which can be improved by changing dosing or formulation or adding oil-free moisturizer.

This is not double blinded study and done in limited population for limited period. Further.

Studies with more number of subjects, long term follow up and microbiological testing would provide more scientific evidence regarding efficacy and safety of nadifloxacin.

5. Conclusion

In the present study, topical antimicrobial agents such as nadifloxacin and clindamycin decreased production of sebum and inflammatory reactions and this study shows that nadifloxacin is as effective as clindamycin and well tolerated, this shows nadifloxacin will be a better alternative for treatment of acne vulgaris.

6. Source of Funding

None.

7. Conflict of Interest

None.


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