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COMPARATIVE STUDY OF TOPICAL OZENOXACIN VS TOPICAL CLINDAMYCIN IN TREATMENT OF ACNE VULGARIS

Dermatology

Dr. Lingaraja M.M Associate Professor, Department of Dermatology, JJMMC, Davangere.
Dr. Rahul H.V* Post Graduate Student, Department of Dermatology, JJMMC, Davangere. *Corresponding Author

ABSTRACT

Background: Topical antimicrobial agents, such as clindamycin and nadifloxacin, are often used to treat inflammatory acne due to their anti-inflammatory effects.Recently, a lotion containing 2% ozenoxacin has shown a good therapeutic effect on patients with acne vulgaris in Japan. Objectives: The objectives of the study was to study efficacy of topical clindamycin and topical ozenoxacin in treatment of acne vulgaris. To Evaluate the side effects of ozenoxacin and clindamycin. Methodology : All patients were subjected to thorough history taking and clinical examination at baseline. Patients were randomized in a 1:1 ratio to receive either topical Clindamycin gel once a day or topical ozenoxacin cream once a day for each lesion for a period of 3 months. **Results & Conclusion :** The effectiveness of Clindamycin and Ozenoxacin treatments on acne was compared. Clindamycin showed decreases in acne severity but MAS score reduction (18 to 13.5) was not significant. Ozenoxacin treatment significantly reduced acne severity with a substantial decrease in the MAS score from 23.5 to 16 ($p<0.05$).

KEYWORDS

Ozenoxacin; Clindamycin; Acne vulgaris.

INTRODUCTION

Acne vulgaris is a chronic, self limiting, inflammatory disease of the pilosebaceous unit. It is the most common skin condition among adolescents and young adults, with a reported prevalence of nearly 80% 1. Its prevalence in this psychologically vulnerable age group, along with its potentially lifelong consequences, makes it a significant financial and psychosocial concern.

Acne is a multifactorial disease influenced by genetic factors, stress, androgens, and excess sweating. Corticosteroids, oral contraceptives, iodides, bromides, lithium, and chemicals such as dioxins are known to induce acne eruptions, as are endocrine disorders such as Cushing's syndrome and polycystic ovary syndrome. It is often found that acne is worse in current smokers.

Propionobacterium acnes colonizes the follicular duct and proliferates, breaking down the sebum into triglycerides, which are irritants that likely contribute to the development of inflammation. When the follicular epithelium is invaded by lymphocytes, it ruptures, releasing sebum, micro-organisms, and keratin into the dermis. Neutrophils, lymphocytes, and foreign body giant cells accumulate and produce the erythematous papules, pustules, and nodular swelling characteristic of inflammatory Acne2

Many medications are available for the management of acne. Antibiotic therapy has been integral to the treatment of acne for many years. The widespread and long-term use of antibiotics has unfortunately led to the emergence of resistant bacteria. Combination therapy with a topical retinoid and an antibiotic is recognized as an effective method for the management of acne vulgaris. The combination of adapalene with oral or topical antibiotics has been shown to release a faster response than an antibiotic alone .

In the other hand, there is significant in-vitro evidence suggesting a possible pathogenetic role for Staphylococcus aureus (S. aureus) in acne vulgaris. Recent advances in the pathogenesis of acne have led to the development of new therapeutic goals. Long-term therapy with oral antibiotic is not only a threat to resistant of P. acne, but also to coagulase negative staphylococci on the skin, S. aureus in the nares, and streptococci in the oral cavity.3

Considering the development of resistance in microorganisms causing acne to antibiotics , more trials is essential to compare the efficacy of newer topical antibiotics.

Topical antimicrobial agents, such as clindamycin and nadifloxacin, are often used to treat inflammatory acne due to their anti-inflammatory effects. For instance, clindamycin has been shown to suppress the production of IL-1β and interferon-γ (IFN-γ) by peripheral blood mononuclear cells (PBMC) stimulated by C. acnes.

Ozenoxacin, a novel nonfluorinated quinolone, has demonstrated a broad antimicrobial spectrum against both Gram-positive and Gram-negative bacteria, including C. acnes. Recently, a lotion containing 2% ozenoxacin (Zebiax Lotion 2%, Maruho Co., Ltd, Osaka, Japan) has shown a good therapeutic effect on patients with acne vulgaris in Japan.4

Hence in this study we are comparing the efficacy of topical ozenoxacin vs topical clindamycin in the treatment of acne vulgaris.

METHODS:

This was a single-centere randomized two-arm parallel-group efficacy trial conducted at the dermatology outpatient department of JJM MEDICAL COLLEGE DAVANGERE between Jun 2023 to April 2024.The study received ethical approval from the Institutional Ethics Committee

Patient selection:

Consecutive patients with acne vulgaris attending the dermatology clinic of this institute were enrolled in this study.

Inclusion criteria:

1) Patients aged more than 12 years

2) A clinical diagnosis of acne vulgaris.

3) Good general health.

4) No use of drugs or other topical medications influencing acne in last two months.

Exclusion criteria:

Before study:

1) Patients who do not give consent

2) Immunosuppressive treatment

3) Pregnancy and Lactation

During study:

1) If patient develops side effects/ intolerance to therapy during treatment.

2) If patient wants to discontinue the treatment.

3) If patient uses any other medication during the study period.

Study protocol

All patients were subjected to thorough history taking and clinical examination at baseline .Patients were randomized in a 1:1 ratio to receive either topical Clindamycin gel once a day or topical ozenoxacin cream once a day for each lesion for a period of 3 months.

Digital photographs were taken after obtaining the consent from

patients. Clinical assessment of acne was performed at the baseline and thereafter at 12 weeks after the completion of treatment protocol .Severity of acne was measured using Michaelson acne score (MAS): which depends on lesion counting and severity index for each lesion: Comedones are valued at 0.5; papules at 1.0; and pustules at 2.0; infiltrates at 3.0; and cysts at 4.0. By multiplying the number of each lesion by its severity index and adding each product we obtain a total score that represents the severity of acne. All adverse effects occurring during the study period as a result of the treatment were also recorded

OBJECTIVES OF THE STUDY:

1) To study efficacy of topical clindamycin and topical ozenoxacin in treatment of acne vulgaris.

2) To Evaluate the side effects of ozenoxacin and clindamycin.

Sample size calculation:

Sample size estimation:

Formula used for sample size calculation

$$n = \frac{Z_{\alpha}^{2} pq}{d^{2}}$$

where,

- Zα: Standard normal deviation equal to 1.96 at 5% level of significance with 95% confidence level.
- p: prevalence =7.1% 9
- q=100-p=100-7.1= 92.9%
- d= allowable error=10%
- Power of the study(1-β)=80
- Considering the non response rate as 10%, the minimum sample size is 29

Statistical Analysis:

The data collected was entered into the excelsheet and was analysed using SPSS version 25.0. Categorical variables were expressed as frequencies(percentages) and quanitative variables as mean±SD and median(IQR). Paired 't' test was applied to check if there was significant difference between MAS scores before and after treatment. P-value<0.05 was considered as statistically significant.

RESULTS

Two treatment groups, Clindamycin (n=23) and Ozenoxacin (n=18), was compared across various variables. In terms of age, the Clindamycin group has a higher mean age (22.6 years) with greater variability (±5.25) compared to the Ozenoxacin group (mean 20.22 years, ±4.58). Both treatment groups are predominantly female, with 65.22% females in the Clindamycin group and 72.22% in the Ozenoxacin group. The Clindamycin group has 34.78% males, while the Ozenoxacin group has 27.78%. The age of disease onset is similar between the groups, with Clindamycin at 19.04 years and Ozenoxacin at 18.56 years. However, there's a difference in disease duration, with Clindamycin-treated patients having a shorter median duration (3 months) compared to Ozenoxacin-treated patients (4.5 months), as indicated by the interquartile range (12 to 18 months for Clindamycin and 3.25 to 12 months for Ozenoxacin). These findings suggest potential differences in treatment efficacy or disease severity between the two groups

Table 1 : Demographic Profile Variables In Clindamycin And Ozenoxacin Group

Variable	Clindamycin (n=23)	Ozenoxacin (n=18)
Age(in years)*	22.6±5.25	20.22±4.58
Sex • Male • Female	 8(34.78) 15(65.22)	 5(27.78) 13(72.22)
Age of onset of disease (in years)*	19.04±3.72	18.56±3.09
Duration of disease (in months)#	3(12,18)	4.5(3.25,12)

*values as mean±SD, #median(IQR)

The table 2 presents aggravating factors in patients treated with Clindamycin (n=23) and Ozenoxacin (n=18). In the Clindamycin group, cosmetics are cited as a significant aggravating factor for 17.39% of patients, whereas in the Ozenoxacin group, this factor affects a much larger proportion, with 77.78% of patients affected. Stress is reported by 39.13% of Clindamycin-treated patients and 38.89% of Ozenoxacin-treated patients, showing similar prevalence between the two groups. Dandruff appears to be more prevalent in the Clindamycin group (65.22%) compared to the Ozenoxacin group (33.33%). Pre-menstrual flare-ups affect 47.83% of Clindamycin-treated patients and 22.22% of Ozenoxacin-treated patients. High-glycemic diet (HGD) and low-glycemic diet (LGD) show similar prevalence between the two groups. Obesity is a rare aggravating factor, reported by only 4.35% of Clindamycin-treated patients and 5.56% of Ozenoxacin-treated patients. Similarly, acanthosis nigricans and polycystic ovary syndrome (PCOS) are infrequent aggravating factors in both groups. These findings suggest that while some aggravating factors may be consistent across treatments, there are notable differences in the prevalence of certain factors, which could influence treatment outcomes and management strategies.

Table 2 : Aggrevating Factors In Clindamycin And Ozenoxacin Groups

Aggrevating factors	Clindamycin (n=23)	Ozenoxacin (n=18)
Cosmetics	4(17.39)	14(77.78)
Stress	9(39.13)	7(38.89)
Dandruff	15(65.22)	6(33.33)
Pre menstrual flare	11(47.83)	4(22.22)
HGD	9(39.13)	7(38.89)
LGD	11(47.83)	5(27.78)
Obesity	1(4.35)	1(5.56)
Acnthosis nigricans	2(8.7)	2(11.11)
PCOD	2(8.7)	1(5.56)

The table 3 compares the effectiveness of Clindamycin treatment and treatment in ozenoxacin on various acne lesions before and after intervention.

For Clindamycin treatment, there are decreases in comedones, papules, and pustules post-treatment, though not statistically significant. The median and mean values for comedones decrease from 10 to 8.5, for papules from 7 to 5.5, and for pustules from 3 to 1 after 12 weeks of treatment. There's no change in nodulocystic lesions. The Median MAS score decreases from 18 to 13.5, but the difference is not statistically significant ($p>0.05$), indicating no significant improvement in overall acne severity.

n contrast, for treatment in ozenoxacin group , there are notable reductions in comedones, papules, and pustules post-treatment, with significant improvement in overall acne severity. The median and mean values for comedones decrease from 11.5 to 10, for papules from 10 to 6.5, and for pustules from 3 to 1 after 12 weeks of treatment .The median MAS score decreases significantly from 23.5 to 16 ($p<0.05$), indicating substantial improvement in overall acne severity post-treatment.

No adverse effects were reported in both the treatment groups

Table 3a : Effectiveness Of Clindamycin Treatment On Various Acne Lesions Before And After Intervention

Variable	Clindamycin			
	Before		After	
	Median (IQR)	Mean ±SD	Median (IQR)	Mean ±SD
Comedones	10 (7.5,11.5)	9.7 ± 4.23	8.5 (6,10)	8.35 ±3.73
Papules	7(6,10)	7.7 ± 3.43	5.5 (4.25,9)	6.32 ±3.48
Pustules	3(2,5)	3.65 ± 2.9	1 (1,2.5)	2.2 ± 2.32
Nodulocystic	0	0	0	0
MAS	18(14,23.25)	20.07±9.13	13.5(11,18)	15.13± 8.24

The difference in MAS score before and after treatment is not statistically significant ($p>0.05$)

Table 3b : Effectiveness Of Treatment In Ozenoxacin On Various Acne Lesions Before And After Intervention

Variable	Ozenoxacin			
	Before		After	
	Median (IQR)	Mean ±SD	Median (IQR)	Mean±SD
Comedones	11.5(9,16)	12.56 ± 6.78	10 (8,15)	11.18 ± 5.91
Papules	10(8,11.75)	10.5 ± 4.03	6.5(5,8)	6.78±3.78
Pustules	3(2,5)	4.611±3.9	1(1,2.75)	2.28±2.69
Nodulocystic	0	0	0	0
MAS	23.5(20,30)	26.56±12.89	16(12,20)	17.53±9.59

The difference in MAS score before and after treatment is statistically

significant ($p<0.05$)

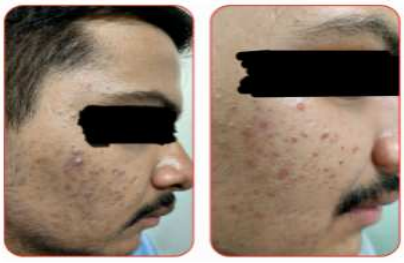


Fig. 1 : MAS score reduction from 23.5 to 14.5 in clinidamycin group

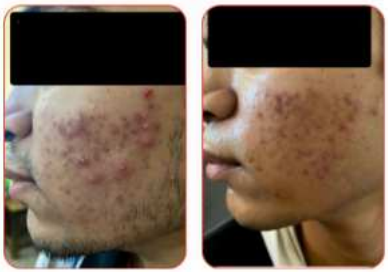
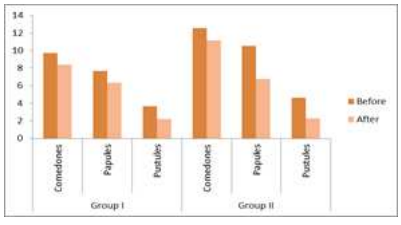


Fig. 2 : MAS score reduction from 35 to 19 in Ozenoxacin group



Group 1 (Clindamycin). Group II (Ozenoxacin)

Fig. 3 : Graph showing Effectiveness of Clindamycin and ozenoxacin treatment on various acne lesions before and after intervention

DISCUSSION

These findings suggest that while Clindamycin treatment effectively targets specific acne symptoms such as papules, and pustules, it may not significantly impact overall acne severity. In contrast, treatment with ozenoxacin leads to significant improvements in both specific symptoms and overall acne severity. This indicates that the treatment utilized in with topical ozenoxacin may be more effective in managing acne compared to Clindamycin treatment.

This is the first study comparing topical Clindamycin and topical ozenoxacin in patients of acne vulgaris. The superior effectiveness of ozenoxacin compared to clindamycin is in accordance to a in vitro study conducted by Akiko Nakajima et al where the antimicrobial activity of ozenoxacin against the clinical isolates of propionibacteria and staphylococci was greater than that of five reference antimicrobial agents which have been used for the treatment of acne vulgaris.[5]

A study by Kanayama S, et al confirmed that ozenoxacin showed a longer-lasting post-antibiotic effect against mutated levofloxacin-susceptible and resistant C. acne compared to other antibacterials [6].In addition, the in vitro and in vivo pharmaceutical and kinetic property profiles of ozenoxacin showed that it is one of the most effective and active drug candidates for controlling bacterial infections.[7]

In a case series by Jena et al where 5 female patients with acne grade 2 were treated with ozenoxacin monotherapy shown excellent response in all 5 patients pretreatment and posttreatment visual analog scale and investigator global assessment scores showed remarkable differences with excellent response in all five patients without any adverse effects.[8]

Overall, understanding the differential effects of treatments on specific acne symptoms and overall severity can inform clinical decision-making and improve patient outcomes in acne management. Further research and clinical trials may be warranted to explore the comparative effectiveness of different treatment modalities in acne management.

CONCLUSION

Ozenoxacin demonstrates superior efficacy in reducing both specific acne symptoms and overall severity compared to Clindamycin, suggesting it may be a more effective treatment option for acne vulgaris. These findings align with prior in vitro studies and highlight the potential for improved clinical outcomes with Ozenoxacin in acne management.

Strength and limitations

1) Limitation is lack of multiple assessor .
2) Patient was not followed up after the treatment period

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