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Clindamycin phosphate, tretinoin with benzoyl peroxide versus clindamycin phosphate and tretinoin combination without benzoyl peroxide for the treatment of acne vulgaris: A comparative study

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***Abstract*---**Introduction: Acne vulgaris (AV) is a prevalent skin disorder among adolescents. Affects around 80–90% of adolescents in the Western population. The present study aimed to compare the therapeutic efficacy of Clindamycin phosphate (CLM), Tretinoin (TN) with Benzoyl peroxide (BP) versus clindamycin phosphate and tretinoin combination without Benzoyl peroxide for treatment of AV. Methodology: 250 patients with mild to moderate acne on the face were enrolled in the study and were divided into two groups; group I (n=125); apply CLM 1.2%, TN 0.025%gel with BP 3.75% gel and group II (n=125) apply only CLM 1.2% and TN 0.025% gel without BP 3.75% gel; once daily at night for 4 weeks. The change in acne lesions was recorded every 2 weekly follow-ups using the global acne grading system and non-inflammatory (NI-L), Inflammatory (I-L) lesions count and Investigator's Static Global Assessment grading. Results: The research involved 250 patients split into two groups: 125 patients in group I and 125 patients in group II. After 4 weeks, the group I had a higher mean percent decrease in non-inflammatory, inflammatory, and total lesion count than group II. Group I performed better on the Global Acne Grading System and Investigator's Static Global Assessment grading observations than group II. Conclusion: This research reveals that the topical combination of clindamycin,

tretinoin, and benzoyl peroxide is more effective than clindamycin and tretinoin alone and gives quick relief from mild to severe acne.

***Keywords*---**clindamycin phosphate, tretinoin, benzoyl peroxide, acne topical preparations, acne antimicrobial treatment.

Introduction

Acne is a persistent inflammation of the pilosebaceous glands. Acne's main and pathognomonic lesion is the small, ocularly-invisible microcomedone.[1] Some microcomedones progress into non-inflammatory lesions (open or closed comedones) or inflammatory lesions (papule, pustule, or nodule).[2] The severity of acne is categorized as mild, moderate, or severe. Mild acne; a few non-inflammatory (comedones) and inflammatory (papulopustular) lesions are present, but no nodulocystic lesions are present. Moderate acne; non-inflammatory lesions predominate, with many inflammatory lesions evident: numerous comedones, papules/pustules, and perhaps one or more tiny nodulocystic lesions.[3] Severe acne; inflammatory lesions are more visible, with several comedones and papules/pustules, and a few nodulocystic lesions may or may not be present.

Acne has a complex etiology, but four fundamental phases have been recognized. These components include hyperproliferation of the follicular epidermis, excessive sebum production, inflammation, and the presence and activity of Propionibacterium acnes.[4] Since the 1980s, acne has been treated using vitamin A retinoid compounds applied topically. They are the most effective comedolytic drugs for treating acne vulgaris because they normalize or even enhance the desquamation process, consequently reducing the production and amount of microcomedones. In addition, they stimulate the elimination of existing comedones and reduce papulopustular lesions. They also have a strong anti-inflammatory impact by suppressing leukocyte activity, the production of pro-inflammatory cytokines and other mediators, and the expression of transcription factors and toll-like receptors involved in immunomodulation. They also assist other active agents in penetrate.[5]

When applied topically, TN, a retinoid produced from naturally occurring trans-retinol (Vitamin A1), reduces follicular epithelium cohesiveness, normalizes keratinocyte desquamation, and accelerates follicular epithelialization cell turnover, producing comedones extrusion.[6] CLM has a direct bacteriostatic and anti-inflammatory action in the pilosebaceous duct against Propionibacterium acnes. In contrast to antimicrobial monotherapy, retinoid and CLM combination treatment had faster and higher effectiveness, presumably owing to the retinoid normalizing desquamation and enabling antimicrobial drug penetration into the subcutaneous follicle.[7] In addition, BP is a bactericidal chemical that may destroy the acne-causing bacteria Propionibacterium acnes. Due to these drugs' complementary modes of action, which effectively target both inflammatory and non-inflammatory acne lesions, adding BP to the TN and CLM treatment schedule may considerably increase the effectiveness of therapy AV.[8,9]. Therefore, we conducted this study to compare the efficacy and tolerability of topical CLM, TN with BP therapy with CLM and TN only to treat mild to moderate acne.

Materials and Methods

From August 2021 to January 2022, this comparative treatment study was done in the outpatient Department of Dermatology at the on-site Tertiary care facility in Chennai, India. The research investigated the effectiveness and safety of topical CLM 1.2%, TN 0.025 % gel with BP 3.75 % gel with CLM 1.2%, and TN 0.025 % gel without BP 3.75 % gel in the treatment of AV. The trial involved 250 participants with mild to severe acne on the face. Before enrolling in the research, all participants gave their informed permission. The Institute's Ethics Committee authorized the research. Each case's diagnosis was based on clinical evidence. 18 to 30-year-old male and female participants were included in the research. Pregnant and lactating females and individuals having a history of hypersensitivity or adverse response to any of the active components of the research medicine were excluded from the study. Patients with hyperandrogenism who simultaneously or concomitantly utilized photosensitizers and acne-causing or -exacerbating medicines were evaluated (e.g., Steroid acne). Patients utilizing systemic antibiotics or retinoids during the last two months or topical acne therapies within the previous two weeks were also excluded.

Examination

Each patient was meticulously checked for acne lesions: -Non inflammatory lesions (NIL); comedones (closed and open). -Inflammatory lesions (IL); papules, pustules, and nodules. According to the Global Acne Grading System (GNGS), the number of lesions on each patient's body was recorded and graded (Table 1). Additionally, Investigator's Static Global Assessment (ISGA) was performed to evaluate the efficacy of AV therapy.[10,11]

Statistical analysis

The observations were assessed statistically using the Chi-square test. A P value of less than <0.0001 was statistically significant.

Results

The demographic characteristics, lesion count, GAGS and ISGA observations were recorded for both groups of subjects (Table 1). The male subjects were observed more in both subjects, 62% in Group I and 57.6% in group II. The average age of patients in both groups was almost similar, 23.86 years in group I and 23.82 years in group II. Most patients reported AV for less than 6 months in both groups, 65 (52%) for group I and 59 (42.4%) for group II patients. Both groups' inflammatory and non-inflammatory lesion counts were also found to be comparable (inflammatory lesion count was 4.11 for group I and 3.87 for group II; non-inflammatory lesion count was 14.26 for group I and 13.92 for group II). Observations of GAGS and ISGA for both patients were reported as comparable. The baseline attribute of the patients of both groups was comparable and could give accurate comparative results of both treatments.

Table 1
Demographic characteristics, lesion count, Global Acne Grading System and Investigator's Static Global Assessment

Patient characteristics		Group I	Group II
Age		23.86±3.59	23.82±3.97
Gender	Male	78 (62%)	72 (57.6%)
	Female	47 (38%)	53 (42.4%)
Duration of acne (months)	<6	65 (52%)	59 (47.2%)
	6-12	34 (27.2%)	39 (31.2%)
	>12	26 (20.8%)	27 (21.6%)
Lesion Count	Inflammatory	4.11±2.61	3.87±2.43
	Non-Inflammatory	14.26±4.80	13.92±3.98
Global Acne Grading System	Mild	13 (10.4%)	9 (7.2%)
	Moderate	92 (73.6%)	97 (77.6%)
	Severe	17 (13.6%)	15 (12%)
	Very Severe	3 (2.4%)	4 (3.2%)
Investigator's Static Global Assessment	Clear (Grade 0)	0	0
	Almost clear (Grade 1)	0	0
	Mild (Grade 2)	12 (9.6%)	9 (7.2%)
	Moderate (Grade 3)	94 (75.2%)	98 (78.4%)
	Severe (Grade 4)	19 (15.2%)	18 (14.4%)

The observation of lesion count, GAGS and IAGS for both patients were reported after 24 weeks of treatment for groups of patients. It was observed that there was a significant decrease in lesion count post-treatment in both groups. The GAGS showed a significant decrease in severe and very severe cases in both groups post treatment. ISGA observation reveals a significant decrease in grade 3 and 4 patients in both groups post-treatment (Tables 2 and 3).

Table 2
Observation of evaluation parameters for group I patient's pre and post treatment

Group I		Pre-treatment	Post-treatment	P value
Lesion Count	Inflammatory	4.11±2.61	0.62±0.51	<0.0001
	Non-Inflammatory	14.26±4.80	3.21±2.94	<0.0001
Global Acne Grading System	Mild	13 (10.4%)	112 (89.6%)	<0.0001
	Moderate	92 (73.6%)	13 (10.4%)	
	Severe	17 (13.6%)	0	
	Very Severe	3 (2.4%)	0	
Investigator's Static Global Assessment	Clear (Grade 0)	0	46 (36.8%)	<0.0001
	Almost clear (Grade 1)	0	61 (48.8%)	
	Mild (Grade 2)	12 (9.6%)	18 (14.4%)	
	Moderate (Grade 3)	94 (75.2%)	0	
	Severe (Grade 4)	19 (15.2%)	0	

Table 3
Observation of evaluation parameters for group II patients pre and post-treatment

Group II		Pre-treatment	Post-treatment	P value
Lesion Count	Inflammatory	3.87±2.43	2.14±1.98	<0.0001
	Non-Inflammatory	13.92±3.98	7.22±4.20	<0.0001
Global Acne Grading System	Mild	9 (7.2%)	89 (71.2%)	<0.0001
	Moderate	97 (77.6%)	28 (22.4%)	
	Severe	15 (12%)	8 (6.4%)	
	Very Severe	4 (3.2%)	0	
Investigator's Static Global Assessment	Clear (Grade 0)	0	21 (16.8%)	<0.0001
	Almost clear (Grade 1)	0	29 (23.2%)	
	Mild (Grade 2)	9 (7.2%)	36 (28.8%)	
	Moderate (Grade 3)	98 (78.4%)	31 (24.8%)	
	Severe (Grade 4)	18 (14.4%)	8 (6.4%)	

All the assessment parameters of both groups were comparatively studied post-treatment. It was observed that Group I patients receiving treatment for CLM, TN and BP showed a significant decrease in lesion count post treatment compared to group II patients receiving treatment for CLM and TN only (Table 4, Fig 1). GAGS and IAGS observations for group I patients were also significantly better than for group II patients after 24 weeks of treatment (Table 4).

Table 4
Comparative observation of Assessment parameters for groups I and II post-treatment

Post-treatment		Group I	Group II	P value
Lesion Count	Inflammatory	0.62±0.51	2.14±1.98	<0.0001
	Non-Inflammatory	3.21±2.94	7.22±4.20	<0.0001
Global Acne Grading System	Mild	112 (89.6%)	89 (71.2%)	<0.0001
	Moderate	13 (10.4%)	28 (22.4%)	
	Severe	0	8 (6.4%)	
	Very Severe	0	0	
Investigator's Static Global Assessment	Clear (Grade 0)	46 (36.8%)	21 (16.8%)	<0.0001
	Almost clear (Grade 1)	61 (48.8%)	29 (23.2%)	
	Mild (Grade 2)	18 (14.4%)	36 (28.8%)	
	Moderate (Grade 3)	0	31 (24.8%)	
	Severe (Grade 4)	0	8 (6.4%)	

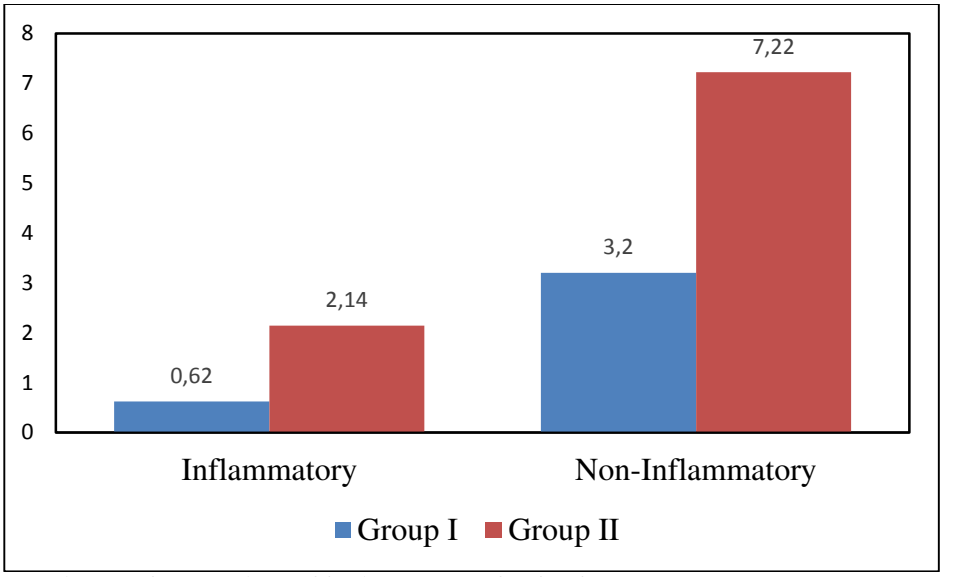

Fig 1. Observation of lesion count for both groups post-treatment

Discussions

AV, which affects 40 to 50 million Americans, is one of the most often seen conditions in dermatology and general care. Acne may affect mental health (such as anxiety and depression), social relationships, self-confidence, self-esteem, and career changes, even in its mildest form.[1,2] Although effective medications and complementary treatments have drastically improved results for many people with severe acne, gains for the far larger group of patients with mild or moderate acne remain elusive. Individualization of treatment and tenacity on the part of both patients and therapists are crucial for this population.[12] In the present study, we compared the efficacy of combination therapy of CLM and TN with BP versus CLM and TN only without BP in treating the mild-moderate AV. This research demonstrated that the combination of CLM 1.2 percent, TN 0.025 percent, and BP 3.75 percent gel is an effective therapy choice for inflammatory and non-inflammatory acne lesions. Combining CLM, TN, and BP was much more effective than CLM and TN alone in reducing acne lesions (inflammatory, non-inflammatory). In patients with moderate to severe acne, the CLM, TN, and BP combo gel was considerably (all p <0.0001) more effective than the same treatment without BP gel in terms of percentage change from baseline to week 24.[13] In this investigation, the percent decrease in acne lesions was greater for the combination group I (71.21–86.33 percent) than in previous clinical trials with the combination of CLM and TN (45.2–65.2%). This study's greater effectiveness in decreasing acne lesion counts might be related to the synergistic effect of combination treatment and the bactericidal effect of BP on the acne-causing Propionibacterium acnes.[14]

In the present study, GAGS was assessed for both groups of patients and it was reported that both groups showed a significant decrease in very severe cases of AV post-treatment (3 Vs 0 for group 1 and 4 Vs 0 for group II). Whereas when both groups were compared, it was found that group CLM, TN and BP therapy

(group I) was significantly better as it further reduced severe cases (17 Vs 0) and moderate cases (92 vs 13). These observations at present are in accordance with previously reported studies.[15] Based on the ISGA score, significantly more patients in group I was verified to be 'clean' or 'nearly clear' of lesions at week 24 than in group II. These findings were similar to those found in another trial with clindamycin and tretinoin. After therapy, no patients in group I had a grade 3 ISGA score (compared to 94 patients at baseline) or a grade 4 ISGA score (compared to 19 patients at baseline). The present study's findings support the previously reported studies, where combination therapy of CLM, TN and BP in acne was more effective and superior to the same therapy without benzoyl peroxide.[16]

Limitations of the study

This study's open-label design and lack of blinding may lead to biased reporting.

Conclusion

This research reveals that the topical combination of CLM, TN, and BP is more effective than CLM and TN alone in treating mild to severe acne and gives quick relief.

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