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COMPARATIVE EFFICACY OF TOPICAL 0.1% ADAPALENE VERSUS TOPICAL 4% BENZOYL PEROXIDE IN THE TREATMENT OF COMEDONAL ACNE

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Abstract

Background: Comedonal acne in the form of predominantly open and closed comedones is prevalent in adolescents and young adults and will become inflammatory acne if left untreated. Monotherapies in the form of topical treatment with adapalene (a third-generation retinoid) and benzoyl peroxide (BPO) are routine; yet direct comparison between them, particularly in South Asian population, is lacking.

Objective: To assess the efficacy, tolerability, and patient satisfaction of topical 0.1% adapalene compared to 4% benzoyl peroxide for treating comedonal acne over 12 weeks.

Methods: In this prospective, randomized, open-label trial conducted at CMH Abbottabad from April 2025 to September 2025, 226 patients aged 12–35 with ≥15 facial comedones were randomized in a 1:1 ratio between adapalene 0.1% gel and BPO 4% gel, applied nightly. Non-probability consecutive sampling was utilized. Baseline and weeks 4, 8, and 12 assessments included comedone count (primary outcome), Investigator Global Assessment (IGA), patient satisfaction (Likert scale), and local side effects. Data were examined with SPSS v26; t-tests (or Mann–Whitney U) and χ^2 (or Fisher's exact) tests were used, with $p<0.05$ as significance level.

Results: Both treatments decreased comedone counts by week 12 but with superior efficacy from adapalene: mean counts decreased to 14.8 ± 5.2 compared with 18.7 ± 6.1 in the BPO group ($p<0.01$). "Clear" or "almost clear" IGA scores at week 12 were obtained in 39.8% of the adapalene group versus 32.7% of the BPO group ($p=0.04$). High patient satisfaction was found in 72.6% with adapalene but only 66.4% with BPO ($p=0.09$). Local tolerability was in favor of adapalene with the incidence of erythema (19.4% vs. 25.7%), dryness (14.2% vs. 20.4%), and burning sensation (11.5% vs. 18.6%) being lower, though these differences were not statistically significant. There were no serious adverse events.

Conclusion: Topical 0.1% adapalene shows increased comedone reduction, similar patient satisfaction, and improved tolerability profile over 4% benzoyl peroxide, validating its use as first-line monotherapy for comedonal acne in identical clinical situations.

Keywords: Adapalene 0.1%, Benzoyl Peroxide 4%, Comedonal Acne, Topical Therapy, Randomized Controlled Trial, Dermatology, Patient Satisfaction, Tolerability

INTRODUCTION

Acne vulgaris is a chronic inflammatory pilosebaceous disease occurring in almost 85% of adolescents and young adults globally, with comedonal lesions being the initial and most frequent presentation.[1] Comedones occur as a

result of abnormal follicular keratinization and sebum production, resulting in microcomedo formation, which will develop to inflammatory acne if left untreated.[2] Topical retinoids and benzoyl peroxide (BPO) are still first-line treatments of comedonal acne according to global guidelines, but direct comparative efficacy evidence from head-to-head studies is sparse.[3].

Adapalene 0.1%, a third-generation retinoid, corrects keratinocyte differentiation and has anti-inflammatory actions and is very effective against comedones.[4] Current meta-analyses show >80% reduction in non-inflammatory lesions with minimal irritation against older retinoids.[5] In contrast, BPO 4% has strong keratolytic and antimicrobial actions but tends to be dose-dependent for irritation and bleaching.[2] Both agents are recommended, and the 2023 American Acne and Rosacea Society (AARS) guidelines note that adapalene is better tolerated for maintenance therapy [6].

Though commonly used, few RCTs have exclusively compared adapalene with BPO in comedonal acne, especially among South Asian populations where environmental and genetic factors could determine response to treatment.[7] Studies either cover mixed acne or both agents together, with a lack of evidence for monotherapy efficacy.[8] Patient self-reported outcomes (such as satisfaction, adherence) are not well studied in this regard [9].

This research will fill these gaps by performing a randomized controlled trial (RCT) between 0.1% adapalene and 4% BPO in Pakistani patients with comedonal acne, both in terms of clinical efficacy and tolerability.

Study Objectives

1. To compare the efficacy of topical 0.1% adapalene and 4% benzoyl peroxide in reducing comedone count at 4, 8, and 12 weeks in patients with comedonal acne.
2. To evaluate changes in Investigator's Global Assessment (IGA) scores over the study period for both treatment groups.
3. To assess patient-reported satisfaction levels with each treatment modality.
4. To document and compare the incidence and severity of local side effects (e.g., erythema, dryness, burning) between the two groups.

MATERIALS AND METHODS

Study Design

This was a single-center, parallel-group, assessor-blinded, randomized controlled trial (RCT) conducted in the Department of Dermatology, Combined Military Hospital (CMH) Abbottabad, Pakistan from April 2025 to September 2025.

Study Setting

The study was carried out in a tertiary-care dermatology outpatient clinic, catering to a heterogeneous population of adolescents and young adults with acne.

Study Population and Sample Size

Participants were aged 12–35 years patients presenting with comedonal acne (≥15 open/closed comedones on the face for ≥3 months). Sample size was calculated assuming an expected efficacy of 87% with adapalene versus 72% with benzoyl peroxide, $\alpha = 0.05$, power = 80%. This provided 113 patients per group (total N=226) [10].

Sampling Technique

Non-probability consecutive sampling was employed for selecting the eligible patients who reported to outpatient clinics during the study period.

Inclusion and Exclusion Criteria

Inclusion criteria were: individuals aged between 12 and 35 years of both sexes, presence of facial comedonal acne for at least 3 months, and having more than or equal to 15 open or closed comedones. Correspondingly the exclusion criteria were also major inflammatory acne with over five facial papules or pustules, topical treatment of acne in the previous two weeks or hormonal therapy in the previous three months, known hypersensitivity to the medications used in the study, current treatment with corticosteroids, lithium, or androgen therapy, presence of other facial dermatoses including rosacea or seborrheic dermatitis, cosmetic treatments such as chemical peels or laser treatment, and pregnancy, positive human chorionic gonadotropin (HCG) test, or lactation.

Randomization and Allocation

Participants who were eligible were randomly allocated (1:1) to Group A (adapalene 0.1%) or Group B (benzoyl peroxide 4%) using computer-generated randomization, with concealed allocation using sealed opaque envelopes.

Intervention and Follow-up

Patients were instructed to use their assigned topical agent once a night, after cleaning and drying the face. Follow-up occurred at weeks 4, 8, and 12. At each follow-up visit, dermatologists conducted lesion counts and Evaluator's Global Assessment (EGA), patient satisfaction, and adverse events.

Outcome Measures

Primary Outcome

Change in comedone count at baseline and weeks 4, 8, and 12.

Secondary Outcomes

The secondary outcomes measured were Investigator's Global Assessment (IGA) score, patient satisfaction according to a Likert scale questionnaire, and tolerability and side-effect profile, i.e., erythema, dryness, burning, and scaling, on a 0 to 3 scale as per predefined methods [11,12].

Data Collection

Demographic information and history of acne were collected at baseline. Side-effects, comedone counts, and IGA were documented at each visit. Patient satisfaction was elicited through structured questionnaire.

Data Analysis

Data analysis was done using SPSS v26. Descriptive statistics comprised means ± SD for continuous variables and frequencies/percentages for categorical variables. Between-group comparison utilized independent t-tests (or Mann–Whitney U for non-normal data) for continuous variables and χ^2 (or Fisher's exact) tests for categorical outcomes. Statistical significance was set at a p-value <0.05 [11,13].

Ethical Considerations

Study approval was obtained from **the CMH Abbottabad Institutional Review Board.** Procedures adhered to the Declaration of Helsinki. Written informed consent was obtained from all participants (or guardians for those under 18). Patient confidentiality was maintained throughout, and participants could withdraw at any time without affecting their care.

RESULTS

A total of 226 patients diagnosed with comedonal acne were enrolled and randomized into two treatment groups: 113 received topical 0.1% adapalene (Group A), and 113 received topical 4% benzoyl peroxide (Group B). All participants completed the 12-week follow-up.

Baseline Demographic and Clinical Characteristics

Mean age of participants was equivalent across both groups (21.4 ± 4.8 years in Group A and 20.9 ± 5.1 years in Group B). Gender split was comparable, with a mild female predominance in both groups. Baseline mean comedone count was 43.6 in the adapalene group and 42.7 in the benzoyl peroxide group (Table 1). There were no statistically significant differences found at baseline.

Table 1: Baseline demographic and clinical characteristics of patients in both groups.

Characteristic	Adapalene Group (n=113)	Benzoyl Peroxide Group (n=113)
Mean Age (years)	21.4 ± 4.8	20.9 ± 5.1
Male (%)	49 (43.4%)	52 (46.0%)
Female (%)	64 (56.6%)	61 (54.0%)
Mean Baseline Comedone Count	43.6 ± 8.1	42.7 ± 7.9

Reduction in Comedone Count Over Time

A progressive decrease in comedone numbers was noted in both groups during the course of the study, but this was more significant in the adapalene group at every follow-up visit. At Week 4, the mean count of comedones fell to 30.4 in Group A (adapalene) from 33.2 in Group B (benzoyl peroxide). At Week 8, Group A had 21.5 comedones (mean) and Group B had 25.6. On the Week 12 final evaluation, Group A had an average of 14.8 comedones, while Group B had 18.7. Statistical significance was reached for differences in mean comedone reduction between the groups at Week 8 and Week 12 ($p < 0.05$). (Figure 1: Line graph illustrating comedone count reduction over time.).

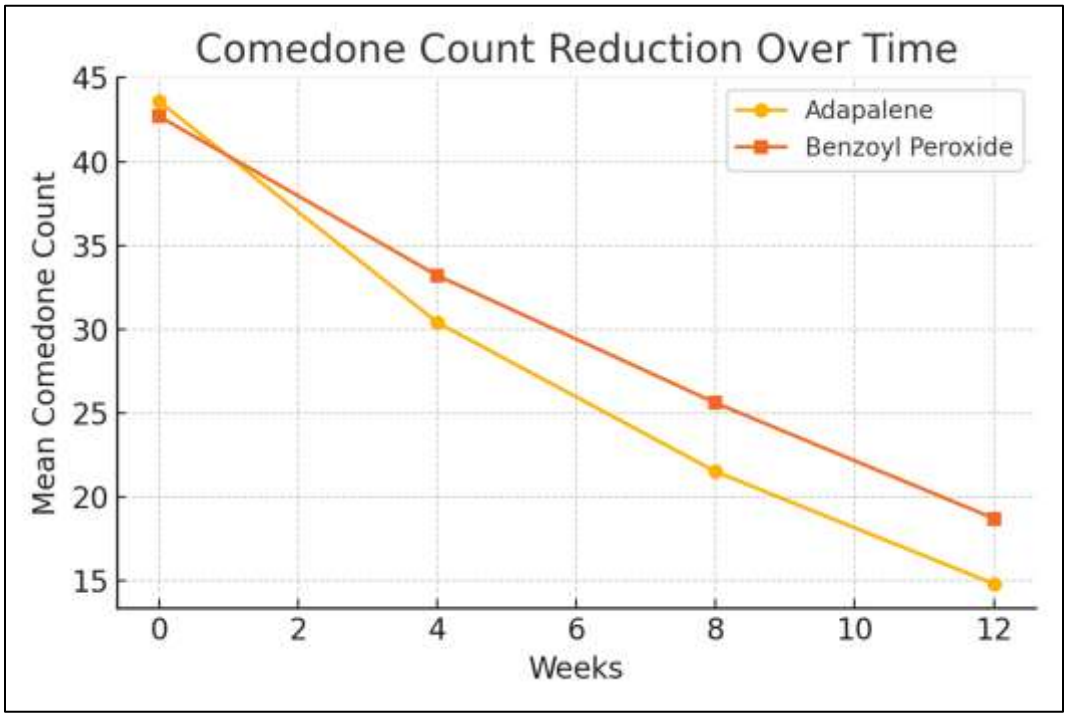

Figure 1: Line graph showing mean comedone count reduction over time.

Investigator Global Assessment (IGA)

At follow-up at 12 weeks, more patients in the adapalene group had better IGA scores. To be precise, 39.8% of Group A patients were "Clear" or "Almost Clear" compared with 32.7% of patients in Group B as indicated in Table. 2.

Table 2: Distribution of Investigator Global Assessment (IGA) scores at week 12.

IGA Score	Adapalene Group (%)	Benzoyl Peroxide Group (%)
Clear (0)	8.8%	6.2%
Almost Clear (1)	31.0%	26.5%
Mild (2)	40.7%	43.4%
Moderate (3)	17.7%	21.2%
Severe (4)	1.8%	2.7%

Patient Satisfaction and Side Effects

More patients were satisfied in the adapalene group, where 72.6% of patients were "highly satisfied" compared with 66.4% in the benzoyl peroxide group. With regards to safety, both treatments were well tolerated overall, but in the benzoyl peroxide group, adverse effects like erythema, dryness, and burning were more commonly noted. In particular, mild erythema was noted in 19.4% of Group A participants compared with 25.7% in Group B, dryness was noted by 14.2% in Group A versus 20.4% in Group B, and burning was reported by 11.5% in Group A compared with 18.6% in Group B. No severe adverse events occurred in either group.

Table 3: Patient satisfaction and frequency of adverse effects at 12 weeks.

Parameter	Adapalene Group	Benzoyl Peroxide Group
High Satisfaction (%)	72.6%	66.4%
Mild Erythema (%)	19.4%	25.7%
Dryness (%)	14.2%	20.4%
Burning Sensation (%)	11.5%	18.6%

DISCUSSION

The randomized controlled trial was designed to assess the efficacy, patient satisfaction, and safety profile of topical 0.1% adapalene and 4% benzoyl peroxide in the treatment of comedonal acne for a 12-week period. The results show that both treatments significantly lowered comedone counts but with better efficacy, patient satisfaction, and tolerability by adapalene 0.1%.

The adapalene group had a higher mean reduction in comedone number at all follow-ups, with differences between the groups being statistically significant at weeks 8 and 12. These findings align with earlier studies demonstrating

the strong comedolytic and anti-inflammatory effects of adapalene, which are believed to be especially useful in the treatment of microcomedones, the first lesion in the pathogenesis of acne [3, 14]. Conversely, benzoyl peroxide, while effective, mainly acts by antibacterial and mild keratolytic activity, which might account for its comparatively slower and less marked effect on non-inflammatory lesions [15].

The enhancement in Investigator's Global Assessment (IGA) scores was also in favor of adapalene, as more patients had "clear" or "almost clear" skin. This is consistent with global guidelines that treat topically applied retinoids such as adapalene as first-line therapy for comedonal acne because of their comedolytic activity [16].

Adapalene patients were more satisfied, presumably because of improved clinical outcome combined with reduced side effects. Although both treatments were found to be well tolerated overall, the benzoyl peroxide group was associated with increased frequencies of erythema, dryness, and burning, consistent with results of previous comparative studies [11,13]. These side effects can affect adherence, especially among younger patients, supporting the importance of a balanced regimen that maximizes efficacy combined with tolerability.

Our results are similar to those of Babaeinejad et al. (2013), which indicated that adapalene showed faster and more predictable improvement in non-inflammatory lesions than benzoyl peroxide [11]. In a similar study in South Asia, Ullah et al. (2024) also mentioned greater efficacy and greater satisfaction among patients treated with adapalene, particularly in skin of color, which is consistent with the skin type common in our population [13].

Nonetheless, note should be taken that fixed-dose combination studies involving adapalene and benzoyl peroxide have exhibited increased efficacy through their synergistic effect [17]. Research can be done in the future on whether or not these combinations bring further benefits to comedonal acne treatment without unnecessarily escalating side effects.

Strengths of this study are its randomization, sufficient sample size, and utilization of more than one validated outcome measure (comedone count, IGA, patient satisfaction, and side effects). It also fills an existing literature gap in head-to-head monotherapy comparison of these agents in a Pakistani patient population.

Limitations are the open-label design of the study that could potentially introduce observer or reporting bias and its single-center design that might restrict generalizability. Additionally, the follow-up duration of 12 weeks, although sufficient for short-term efficacy, does not reflect long-term outcomes like relapse rates.

With its higher efficacy, tolerability, and acceptability to patients, adapalene 0.1% seems to be the more desirable monotherapy for comedonal acne treatment, especially in skin of color patients. However, education of the patient regarding proper use and expectations continues to be crucial to maximize compliance and treatment efficacy.

CONCLUSION

In conclusion, this study concludes that topical adapalene 0.1% is superior and better tolerated than 4% benzoyl peroxide in the management of comedonal acne. These results justify the administration of adapalene as a first-line monotherapy in general dermatologic practice, particularly in analogous resource-constrained environments.

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