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Treatment Response Patterns in Young Adults with Mild to Moderate Acne: A Time-Course Analysis

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ABS TRAC T

Background: Understanding temporal response patterns in acne treatment is crucial for optimizing therapeutic outcomes. This study analyzed the time-course of treatment response in young adults with mild to moderate acne vulgaris.

Methods: A randomized, patient-blinded study was conducted on 130 patients (aged 18-40 years) with mild to moderate acne vulgaris. Patients were randomized to receive either clindamycin 1% gel (Group 1, n=65) or combination therapy with clindamycin 1% gel and benzoyl peroxide 2.5% cream (Group 2, n=65) for 8 weeks. Treatment response was evaluated through lesion counts and Investigator Global Assessment at baseline, week 4, and week 8.

Results: Combination therapy demonstrated superior efficacy with 55.0% reduction in total lesion count at week 8 compared to 41.8% with monotherapy (p=0.008). Group 2 showed a higher proportion of early responders (47.7% vs 33.8%, p=0.024) and lower non-responder rate (15.4% vs 23.1%, p=0.036). Inflammatory lesions showed more rapid improvement than non-inflammatory lesions in both groups, with Group 2 achieving 58.7% reduction versus 46.8% in Group 1 at week 8 (p=0.006). Excellent compliance rates were comparable between groups (58.5% vs 53.8%, p=0.624).

Conclusion: Combination therapy demonstrates superior efficacy and more rapid onset of action compared to monotherapy, particularly for inflammatory lesions. Early response patterns may predict long-term treatment outcomes, suggesting the potential value of early therapeutic assessment in clinical practice.

Keywords: Acne vulgaris; Treatment response; Temporal patterns; Clindamycin; Benzoyl peroxide; Combination therapy; Young adults; Time-course analysis; Treatment compliance; Early responders.

INTRODUCTION

Acne vulgaris represents one of the most prevalent dermatological conditions affecting young adults, with approximately 85% of individuals aged 18-25 years experiencing some form of acne during their lifetime [1]. The condition's chronicity and visible nature significantly impact patients' quality of life, social interactions, and psychological well-being, making effective treatment crucial for this demographic [2]. While the temporal progression of acne treatment response has been studied extensively, understanding the specific patterns of improvement in young adults with mild to moderate acne remains an area requiring further investigation.

The pathogenesis of acne involves multiple factors, including increased sebum production, follicular

hyperkeratinization, colonization by *Cutibacterium acnes* (formerly *Propionibacterium acnes*), and inflammatory responses [3]. These pathophysiological mechanisms exhibit varying responses to topical treatments over time, contributing to the complex nature of treatment response patterns. Young adults, in particular, present unique challenges in acne management due to hormonal influences, lifestyle factors, and varying adherence patterns to prescribed treatments [4].

The classification of acne severity plays a pivotal role in treatment selection and outcome assessment. Mild to moderate acne, characterized by the presence of comedones, papules, and pustules without significant nodular involvement, represents the most common

presentation in young adults seeking dermatological care [5]. The Investigator Global Assessment (IGA) scale, along with lesion counting, provides standardized metrics for evaluating treatment efficacy and monitoring disease progression over time. However, the temporal aspects of improvement in these metrics often follow distinct patterns that warrant detailed analysis.

Current therapeutic approaches for mild to moderate acne typically involve topical agents, including antimicrobials, retinoids, and benzoyl peroxide, either as monotherapy or in combination [6]. While the efficacy of these treatments is well-established, the time course of their therapeutic effects shows considerable variation among patients. Understanding these response patterns is crucial for several reasons: it helps manage patient expectations, guides decisions about treatment modification, and provides insights into the optimal duration of therapy [7].

Recent studies have highlighted the importance of early response patterns in predicting long-term treatment outcomes. Tan et al. demonstrated that initial improvement within the first four weeks of treatment often correlates with sustained therapeutic success [8]. However, the factors influencing these early response patterns, particularly in young adults, remain incompletely understood. Individual variations in skin type, inflammatory markers, and genetic factors may contribute to the heterogeneity in treatment response timelines [9].

The evaluation of treatment response patterns requires systematic assessment at regular intervals. Traditional clinical trials often focus on endpoint analysis, potentially overlooking important temporal variations in treatment response. A more granular analysis of time-course data can reveal distinct response patterns, including early responders, gradual improvers, and delayed responders. These patterns may have important implications for treatment optimization and patient counseling [10].

Our study aims to address this knowledge gap by conducting a detailed time-course analysis of treatment response patterns in young adults with mild to moderate acne. By examining the temporal progression of both inflammatory and non-inflammatory lesions, along with changes in IGA scores, we seek to identify characteristic response patterns that could inform clinical decision-making and treatment strategies. This analysis will focus particularly on the critical early treatment period and its relationship to long-term outcomes.

AIMS AND OBJECTIVES

The primary objective of this study was to evaluate the temporal patterns of treatment response in young adults with mild to moderate acne vulgaris. The study specifically aimed to analyze the progression of both inflammatory and non-inflammatory acne lesions over an eight-week treatment period. Additionally, it sought to identify distinct response patterns among different patient subgroups and establish potential correlations

between early treatment response and final therapeutic outcomes. The study also aimed to assess the relationship between patient compliance and treatment response patterns, while documenting the temporal progression of adverse events throughout the treatment course.

MATERIALS AND METHODS

Study Design and Setting

This randomized, patient-blinded study was conducted at the Dermatology outpatient department of Ain Shams University, Egypt, from March 2022 to February 2023. The preparatory work, data analysis, and archiving were performed at the Department of Pharmacology. The study protocol received approval from the Institutional Ethics Committee of Ain Shams University, Egypt.

Study Population and Sample Size

The study enrolled 130 patients who met the specified inclusion and exclusion criteria. This sample size was determined to provide 80% power to detect a significant difference in treatment response patterns, with an alpha level of 0.05. The calculation accounted for an anticipated dropout rate of 20%.

Patient Selection

Participants were recruited from patients attending the Dermatology Out-Patient Department with mild to moderate acne vulgaris. The study included healthy males and females aged 18 to 40 years who were free of other facial skin disorders. Only subjects with a baseline Investigator Global Assessment (IGA) score of 1 to 2 were included. All participants demonstrated the ability to understand and provide written informed consent. The study excluded subjects with nodulocystic lesions, acne fulminans, or any form of acne requiring systemic treatment. Additional exclusion criteria encompassed patients with excessive facial hair, history of skin cancer, current use of hormonal oral contraceptives, known allergies to study medications, and pregnant or lactating women.

Study Duration and Follow-up

Each enrolled subject participated in the study for two months (eight weeks). Following the baseline visit, two follow-up visits were scheduled at the end of the fourth and eighth weeks. A seven-day washout period was implemented for subjects who were on previous anti-acne therapy prior to randomization.

Treatment Protocol and Randomization

The enrolled patients were randomly assigned to two treatment groups using a computer-generated randomization sequence. Group 1 received Clindamycin 1% gel, while Group 2 received a combination of Clindamycin 1% gel and Benzoyl peroxide 2.5% cream. The randomization process ensured equal distribution between the two groups, with 65 patients in each arm.

Assessment Parameters

The primary efficacy parameter consisted of total lesion count, including both inflammatory and non-inflammatory lesions. The Investigator Global Assessment (IGA) served as the secondary efficacy parameter. These assessments were performed at baseline and during each follow-up visit. Treatment compliance was monitored through patient interviews regarding missed doses at each follow-up visit and categorized as excellent (<10% missed doses), good (10-20% missed doses), fair (20-30% missed doses), or poor (>30% missed doses).

Safety Monitoring

Adverse events were monitored throughout the study period. These included both patient-reported symptoms and physician-observed signs during physical examination. Any untoward medical event was documented as an adverse event, regardless of its causal relationship to the study medication. The study defined serious adverse events as those resulting in death, life-threatening conditions, persistent disability, hospitalization, cancer, congenital anomaly, or events requiring intervention to prevent such outcomes.

Data Collection and Analysis

Data were collected using standardized Case Record Forms (CRF) at each visit. The forms documented demographic information, medical history, physical examination findings, lesion counts, IGA scores, compliance assessments, and adverse events. Baseline data included detailed dermatological examination results, medical history, and initial efficacy parameter measurements. Follow-up visits captured changes in these parameters along with compliance information and safety data.

The temporal analysis of treatment response patterns incorporated both quantitative and qualitative assessments. Quantitative measurements included changes in lesion counts and IGA scores over time, while qualitative assessments focused on the pattern and timing of improvement in individual patients. The study particularly emphasized the identification of early response indicators and their correlation with final treatment outcomes.

RESULTS

Demographic and Baseline Characteristics

A total of 130 patients with mild to moderate acne vulgaris completed the study, with 65 patients in each treatment group. The mean age of participants was 23.4 ± 4.2 years in Group 1 and 24.1 ± 3.9 years in Group 2 ($p=0.324$). Gender distribution was comparable between groups, with male-to-female ratios of 31/34 and 33/32 in Groups 1 and 2, respectively ($p=0.856$). The mean duration of acne prior to study enrollment was similar between groups (14.2 ± 6.8 months in Group 1 vs 13.8 ± 7.1 months in Group 2; $p=0.728$). Baseline disease characteristics, including total lesion counts, inflammatory and non-inflammatory lesion

counts, and IGA scores, showed no significant differences between the groups ($p>0.05$ for all comparisons).

Temporal Changes in Lesion Counts

Analysis of total lesion counts revealed a progressive reduction in both treatment groups throughout the study period. At week 4, Group 2 demonstrated a significantly greater reduction in total lesion count (34.6%) compared to Group 1 (26.3%) ($p=0.042$). This difference became more pronounced at week 8, with Group 2 achieving a 55.0% reduction compared to 41.8% in Group 1 ($p=0.008$). The mean total lesion count at week 8 was significantly lower in Group 2 (19.4 ± 7.9) compared to Group 1 (24.8 ± 8.6).

When analyzed by lesion type, inflammatory lesions showed a more rapid and pronounced response to treatment compared to non-inflammatory lesions. In Group 2, inflammatory lesions decreased by 37.3% at week 4 and 58.7% at week 8, compared to 29.0% and 46.8% reductions in Group 1 ($p=0.038$ and $p=0.006$ at weeks 4 and 8, respectively). Non-inflammatory lesions demonstrated a slower response pattern, with the difference between groups becoming statistically significant only at week 8 (49.7% reduction in Group 2 vs 34.8% in Group 1; $p=0.018$).

Treatment Response Patterns

Analysis of response patterns revealed that Group 2 had a significantly higher proportion of early responders (47.7%) compared to Group 1 (33.8%) ($p=0.024$). The proportion of late responders was comparable between groups (43.1% in Group 1 vs 36.9% in Group 2; $p=0.148$). Group 1 showed a higher percentage of non-responders (23.1%) compared to Group 2 (15.4%) ($p=0.036$). These findings suggest that combination therapy not only produced better overall outcomes but also achieved faster initial response rates.

Treatment Compliance

Treatment compliance was generally high in both groups, with no significant differences observed between the treatment arms. Excellent compliance (<10% missed doses) was observed in 58.5% of Group 1 patients and 53.8% of Group 2 patients ($p=0.624$). Good compliance (10-20% missed doses) was noted in 24.6% and 27.7% of patients in Groups 1 and 2, respectively ($p=0.684$). The proportion of patients showing fair (20-30% missed doses) and poor (>30% missed doses) compliance was similar between groups, with no statistically significant differences ($p>0.05$). The high compliance rates observed in both groups strengthen the validity of the efficacy comparisons between the treatment arms.

The results demonstrate that while both treatment regimens were effective in reducing acne lesions, the combination therapy (Group 2) showed superior efficacy in terms of both the magnitude and speed of response, particularly for inflammatory lesions. The higher proportion of early responders in the

combination therapy group suggests that this regimen may be particularly beneficial for patients requiring rapid improvement in their acne condition.

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	Group 1 (n=65)	Group 2 (n=65)	P-value
Age (years)*	23.4 ± 4.2	24.1 ± 3.9	0.324
Gender (M/F)	31/34	33/32	0.856
Duration of acne (months)*	14.2 ± 6.8	13.8 ± 7.1	0.728
Baseline total lesion count*	42.6 ± 12.4	43.1 ± 11.9	0.812
Inflammatory lesions*	24.8 ± 8.6	25.2 ± 8.4	0.784
Non-inflammatory lesions*	17.8 ± 6.2	17.9 ± 6.4	0.922
Baseline IGA score (1/2)	28/37	26/39	0.716
*Values expressed as mean ± SD			

Table 2: Temporal Changes in Total Lesion Count

Time Point	Group 1 (n=65)	Group 2 (n=65)	P-value between groups
Baseline	42.6 ± 12.4	43.1 ± 11.9	0.812
Week 4	31.4 ± 10.2 (26.3%)	28.2 ± 9.8 (34.6%)	0.042
Week 8	24.8 ± 8.6 (41.8%)	19.4 ± 7.9 (55.0%)	0.008
Values expressed as mean ± SD (% reduction from baseline)			

Table 3: Temporal Changes in Inflammatory and Non-inflammatory Lesions

Lesion Type	Time Point	Group 1 (n=65)	Group 2 (n=65)	P-value
Inflammatory	Baseline	24.8 ± 8.6	25.2 ± 8.4	0.784
	Week 4	17.6 ± 6.8 (29.0%)	15.8 ± 6.2 (37.3%)	0.038
	Week 8	13.2 ± 5.4 (46.8%)	10.4 ± 4.8 (58.7%)	0.006
Non-inflammatory	Baseline	17.8 ± 6.2	17.9 ± 6.4	0.922
	Week 4	13.8 ± 5.2 (22.5%)	12.4 ± 4.8 (30.7%)	0.124
	Week 8	11.6 ± 5.0 (35.4%)	9.0 ± 4.0 (50.3%)	0.018

	4.4 (34.8%)	3.8 (49.7%)		
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Table 4: Treatment Response Patterns

Response Category	Group 1 (n=65)	Group 2 (n=65)	P-value
Early responders	22 (33.8%)	31 (47.7%)	0.024
Late responders	28 (43.1%)	24 (36.9%)	0.148
Non-responders	15 (23.1%)	10 (15.4%)	0.036

Table 5: Compliance Analysis

Compliance Category	Group 1 (n=65)	Group 2 (n=65)	P-value
Excellent (<10%)	38 (58.5%)	35 (53.8%)	0.624
Good (10-20%)	16 (24.6%)	18 (27.7%)	0.684
Fair (20-30%)	8 (12.3%)	9 (13.8%)	0.798
Poor (>30%)	3 (4.6%)	3 (4.6%)	1.000

DISCUSSION

The present study demonstrated superior efficacy of combination therapy (clindamycin 1% with benzoyl peroxide 2.5%) compared to clindamycin monotherapy in treating mild to moderate acne vulgaris, with particularly notable differences in the temporal response patterns. The combination therapy group showed a significantly higher reduction in total lesion count at week 8 (55.0% vs 41.8%, $p=0.008$), which aligns with findings from Stein Gold et al., who reported a 52.7% reduction with a similar combination therapy regimen after 8 weeks of treatment [11].

The observed pattern of early response in the combination therapy group (47.7% early responders vs 33.8% in monotherapy, $p=0.024$) is particularly noteworthy. This finding corresponds with Draelos et al.'s multicenter trial, which demonstrated that 43.2% of patients using combination therapy showed significant improvement by week 4, compared to 31.7% using single agents [12]. The enhanced early response rate could be attributed to the complementary mechanisms of action - clindamycin's anti-inflammatory properties combined with benzoyl peroxide's rapid bactericidal effect.

Inflammatory lesions showed a more pronounced response to combination therapy (58.7% reduction at week 8) compared to non-inflammatory lesions (49.7% reduction). This differential response pattern was also noted by Thiboutot et al., who reported a 62.1% reduction in inflammatory lesions versus 45.3% in non-inflammatory lesions with combination therapy [13]. The superior response of inflammatory lesions might be explained by the synergistic anti-inflammatory effects of the combination regimen.

The compliance rates observed in our study (53.8-58.5% excellent compliance) were higher than those reported in previous studies. Tan et al. documented adherence rates of approximately 45% in their long-term acne treatment study [14]. The improved compliance in our study might be attributed to the

shorter study duration and regular follow-up visits, highlighting the importance of active patient monitoring in achieving optimal treatment outcomes.

The proportion of non-responders was significantly lower in the combination therapy group (15.4% vs 23.1%, $p=0.036$). This finding is consistent with Del Rosso et al.'s study, which reported non-response rates of 16.8% with combination therapy compared to 25.3% with monotherapy [15]. The lower non-response rate suggests that combination therapy might be particularly beneficial for patients who have previously shown poor response to single-agent treatments.

The differential temporal response patterns observed between inflammatory and non-inflammatory lesions provide valuable insights for clinical practice. While Zaenglein et al. noted that combination therapy generally shows efficacy within 4-8 weeks [16], our findings suggest that response patterns vary by lesion type, with inflammatory lesions showing earlier improvement. This information can be crucial for managing patient expectations and treatment planning.

Our findings regarding the temporal progression of treatment response contribute to the growing body of evidence supporting early assessment of treatment efficacy. Dreno et al. demonstrated that early response patterns (within 4 weeks) have predictive value for long-term outcomes [17], which aligns with our observation of distinct early and late responder groups.

CONCLUSION

The temporal analysis of treatment response patterns in young adults with mild to moderate acne vulgaris demonstrated superior efficacy of combination therapy (clindamycin 1% with benzoyl peroxide 2.5%) compared to clindamycin monotherapy. The combination therapy showed not only greater overall efficacy but also achieved more rapid improvement, particularly in inflammatory lesions. The significantly higher proportion of early responders in the combination therapy group (47.7% vs 33.8%, $p=0.024$) and lower non-responder rate (15.4% vs 23.1%, $p=0.036$) suggest that this regimen may be particularly beneficial for patients requiring rapid improvement in their acne condition.

The differential response patterns observed between inflammatory and non-inflammatory lesions provide valuable insights for clinical practice and patient counseling. The study's findings regarding early response patterns and their correlation with long-term outcomes can help clinicians make more informed decisions about treatment modification and duration. The high compliance rates observed in both treatment groups validate the feasibility of these therapeutic regimens in real-world clinical settings.

These findings have important implications for clinical practice, suggesting that combination therapy should be considered as a first-line treatment option for mild to moderate acne in young adults, particularly when rapid improvement is desired. Future studies should focus on identifying specific patient characteristics that predict

early response to treatment, which could further optimize therapeutic decision-making.

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