

## COMPARATIVE STUDY ON THE EFFICACY OF TOPICAL VS ORAL TREATMENTS IN MANAGING ACNE VULGARIS, REVIEW OF THERAPEUTIC OUTCOMES AND PATIENT RESPONSES

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### Abstract

**Background:** Acne vulgaris is a chronic inflammatory skin disorder associated with significant physical, psychological, and quality-of-life impairment. Although topical and systemic therapies are widely used for moderate-to-severe acne, comparative evidence evaluating their efficacy, safety, and impact on quality of life remains limited.

**Objective:** To compare the clinical efficacy, safety profile, and quality-of-life outcomes of topical therapy versus systemic therapy in patients with moderate-to-severe acne vulgaris.

**Methods:** A prospective, randomized, single-blind study was conducted among 360 patients aged 16–40 years with moderate or severe acne vulgaris. Participants were randomized into three groups: topical therapy, systemic therapy, and combination therapy. Clinical outcomes were assessed using Investigator's Global Assessment (IGA), lesion count reduction, Dermatology Life Quality Index (DLQI), and Acne-QoL scores over 24 weeks.

**Results:** All treatment groups showed significant clinical improvement. Systemic and combination therapies resulted in significantly greater reductions in inflammatory and total lesion counts compared with topical therapy alone ( $p < 0.001$ ). Combination therapy achieved the highest IGA success rate (78.3%). Quality-of-life scores improved significantly across all groups and correlated positively with clinical improvement. Topical therapy demonstrated superior tolerability.

**Conclusion:** Systemic therapy provides greater short-term efficacy in moderate-to-severe acne, while topical therapy offers a safer alternative. Combination therapy yields optimal clinical and quality-of-life outcomes. Individualized treatment selection is essential.

**Keywords:** Acne vulgaris, topical therapy, systemic therapy, doxycycline, quality of life

## СРАВНИТЕЛЬНОЕ ИССЛЕДОВАНИЕ ЭФФЕКТИВНОСТИ МЕСТНЫХ И ПЕРОРАЛЬНЫХ МЕТОДОВ ЛЕЧЕНИЯ УГРЕВОЙ СЫПИ: ОБЗОР ТЕРАПЕВТИЧЕСКИХ РЕЗУЛЬТАТОВ И РЕАКЦИИ ПАЦИЕНТОВ

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### Аннотация

**Введение:** Угревая сыпь — это хроническое воспалительное заболевание кожи, связанное со значительным ухудшением физического, психологического состояния и

качества жизни. Хотя местные и системные методы лечения широко используются при угревой сыпи средней и тяжелой степени, сравнительные данные об их эффективности, безопасности и влиянии на качество жизни остаются ограниченными.

**Цель:** Сравнить клиническую эффективность, профиль безопасности и показатели качества жизни при местной и системной терапии у пациентов с акне средней и тяжелой степени.

**Методы:** Было проведено проспективное рандомизированное одностороннее исследование с участием 360 пациентов в возрасте 16–40 лет с акне средней или тяжелой степени. Участники были рандомизированы на три группы: местная терапия, системная терапия и комбинированная терапия. Клинические результаты оценивались с использованием глобальной оценки исследователя (IGA), уменьшения количества поражений, индекса качества жизни при дерматологических заболеваниях (DLQI) и показателей качества жизни при акне (Acne-QoL) в течение 24 недель.

**Результаты:** Во всех группах лечения наблюдалось значительное клиническое улучшение. Системная и комбинированная терапия привели к значительно большему уменьшению количества воспалительных и общих поражений по сравнению с одной только местной терапией ( $p < 0,001$ ). Комбинированная терапия достигла наивысшего показателя успеха по шкале IGA (78,3%). Показатели качества жизни значительно улучшились во всех группах и положительно коррелировали с клиническим улучшением. Местная терапия продемонстрировала лучшую переносимость.

**Вывод:** Системная терапия обеспечивает большую краткосрочную эффективность при акне средней и тяжелой степени, в то время как местная терапия является более безопасной альтернативой. Комбинированная терапия обеспечивает оптимальные клинические результаты и улучшение качества жизни. Индивидуальный выбор лечения имеет важное значение.

**Ключевые слова:** Акне обыкновенное, местная терапия, системная терапия, доксициклин, качество жизни

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## Introduction

Acne vulgaris is one of the most common chronic inflammatory skin disorders worldwide, affecting approximately 85% of adolescents and a substantial proportion of adults [1,2]. Although traditionally considered a benign and self-limiting condition of adolescence, acne is now recognized as a persistent disease with significant physical, psychological, and social consequences. The condition frequently extends into adulthood, particularly among women, contributing to long-term morbidity [3].

The pathogenesis of acne is multifactorial and involves follicular hyperkeratinization, increased sebum production, colonization by *Cutibacterium acnes*, and a complex inflammatory response [4]. These mechanisms result in inflammatory and non-inflammatory lesions that may lead to permanent scarring if inadequately treated [5]. Beyond its cutaneous manifestations, acne has been associated with increased rates of anxiety, depression,

reduced self-esteem, and social withdrawal, significantly impairing quality of life [6–8]. The psychosocial burden of acne has been reported to be comparable to that of chronic systemic diseases [8].

Management of acne aims to target multiple pathogenic factors while minimizing adverse effects and preventing antibiotic resistance. International guidelines recommend topical combination therapy for moderate acne and systemic therapy, particularly oral antibiotics, for more severe disease [11,12]. Systemic agents are known to provide faster and more pronounced reductions in inflammatory lesions; however, their use is limited by potential adverse effects, concerns regarding antimicrobial resistance, and long-term safety [13,14].

Despite the widespread use of both topical and systemic therapies, direct comparative studies assessing their relative efficacy, safety, and impact on patient-reported outcomes in moderate-to-severe acne remain limited. Furthermore, few studies have evaluated clinical improvement alongside validated quality-of-life measures. Therefore, this study was designed to compare the efficacy, safety, and quality-of-life outcomes of standardized topical therapy versus systemic therapy, with and without combination treatment, in patients with moderate-to-severe acne vulgaris.

## Materials and Methods

### *Study Design and Setting*

This prospective, randomized, single-blind comparative study was conducted at the Department of Dermatology, S. B. Daniyarov South Branch of Kyrgyz State Medical Institute, in accordance with the Declaration of Helsinki.

### *Participants*

Patients aged 16–40 years with moderate (IGA 3) or severe (IGA 4) acne vulgaris were enrolled. Exclusion criteria included pregnancy, recent acne treatment, hypersensitivity to study medications, and severe nodulocystic acne requiring isotretinoin.

### *Randomization and Interventions*

A total of 360 eligible participants were randomized equally into three groups:

Topical therapy group: Adapalene 0.1% and benzoyl peroxide 2.5% gel once daily

Systemic therapy group: Doxycycline 100 mg daily ± spironolactone (in females), with benzoyl peroxide wash

Combination therapy group: Both topical and systemic regimens

### *Outcome Measures*

Primary outcomes included percentage reduction in lesion counts and IGA success ( $\geq 2$ -grade improvement). Secondary outcomes included DLQI, Acne-QoL scores, and adverse events.

### *Statistical Analysis*

Statistical analysis was performed using SPSS software. Continuous variables were analyzed using repeated-measures ANOVA, and categorical variables using chi-square tests. A p-value  $< 0.05$  was considered statistically significant.

## Results

### *Participant Flow and Baseline Characteristics*

A total of 415 patients were screened, of whom 360 participants met the eligibility criteria and were randomized equally into three groups: topical therapy (n=120), systemic therapy (n=120), and combination therapy (n=120). Overall study completion was high (91.7%), with comparable dropout rates across groups. The Intention-to-Treat (ITT) population included all randomized participants.

Baseline demographic and clinical characteristics were well balanced across the three groups, confirming successful randomization (Table 1). The mean age of participants was  $21.8 \pm 4.5$  years, with females constituting approximately 60% of the cohort. Approximately 65% of participants presented with moderate acne (IGA 3), while 35% had severe acne (IGA 4).

• *Table 1. Baseline Demographic and Clinical Characteristics*

Characteristic	Topical (n=120)	Systemic (n=120)	Combination (n=120)	p-value
Age (years, mean $\pm$ SD)	$21.5 \pm 4.1$	$22.1 \pm 5.0$	$21.7 \pm 4.3$	0.642
Female, n (%)	72 (60.0)	74 (61.7)	70 (58.3)	0.901
IGA 4 (Severe), n (%)	42 (35.0)	45 (37.5)	39 (32.5)	0.834
Total lesion count	$73.7 \pm 16.9$	$73.6 \pm 17.2$	$74.4 \pm 17.8$	0.937
DLQI score	$12.5 \pm 3.2$	$11.9 \pm 3.5$	$12.8 \pm 3.1$	0.118

### **Reduction in Lesion Counts**

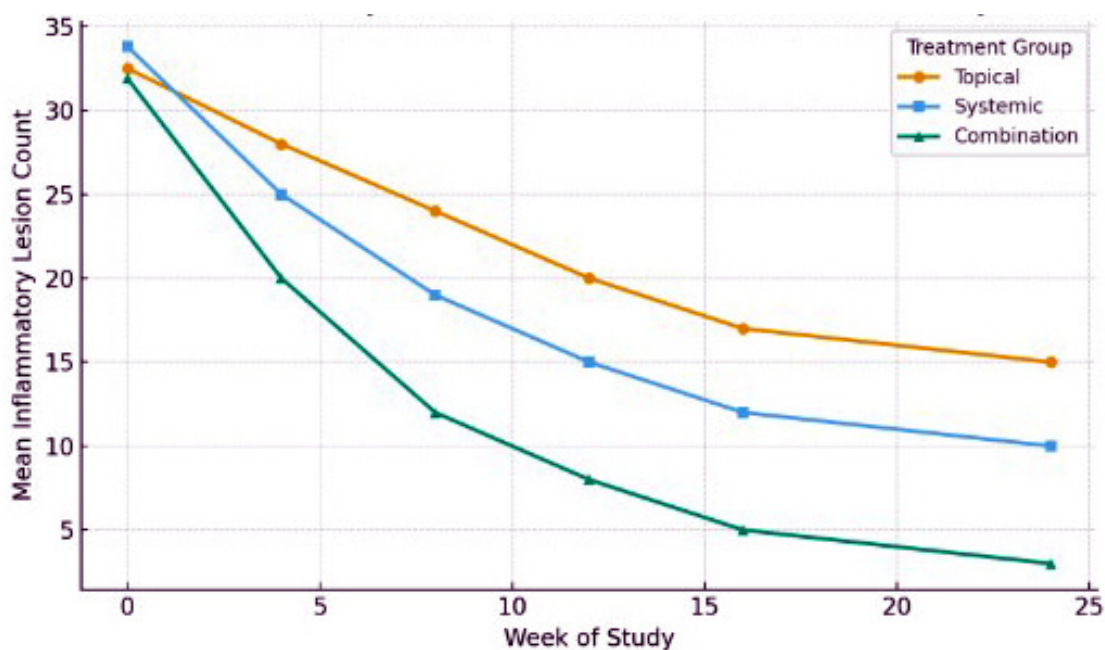
All treatment groups showed statistically significant reductions in inflammatory, non-inflammatory, and total lesion counts from baseline to week 24 ( $p < 0.001$  for all within-group comparisons). However, the magnitude and speed of response differed significantly between groups.

At week 24, the combination therapy group demonstrated the greatest mean percentage reduction in inflammatory lesions (84.6%), followed by the systemic group (72.1%) and topical group (58.3%) ( $p < 0.001$ ). Similar trends were observed for non-inflammatory and total lesion counts (Table 2).

• *Table 2. Mean Percentage Reduction in Lesion Counts at Week 24*

Lesion Type	Topical (%)	Systemic (%)	Combination (%)	p-value
Inflammatory	$58.3 \pm 16.1$	$72.1 \pm 14.5$	$84.6 \pm 10.2$	$<0.001$
Non-inflammatory	$49.7 \pm 18.3$	$61.2 \pm 15.8$	$78.9 \pm 12.7$	$<0.001$
Total lesions	$53.4 \pm 15.9$	$66.2 \pm 14.2$	$81.5 \pm 10.5$	$<0.001$

• Figure 1. Mean inflammatory lesion count over 24 weeks study period



#### Investigator's Global Assessment (IGA) Success

At the primary endpoint (week 24), IGA treatment success (score 0 or 1) was achieved by: 78.3% of participants in the combination group

- 65.8% in the systemic group
- 45.0% in the topical group

The differences were statistically significant ( $p < 0.001$ ), with all pairwise comparisons remaining significant after Bonferroni correction.

• Table 3. IGA Treatment Success Rates

Time Point	Topical	Systemic	Combination	p-value
Week 12	25.0%	45.8%	62.5%	<0.001
Week 24	45.0%	65.8%	78.3%	<0.001

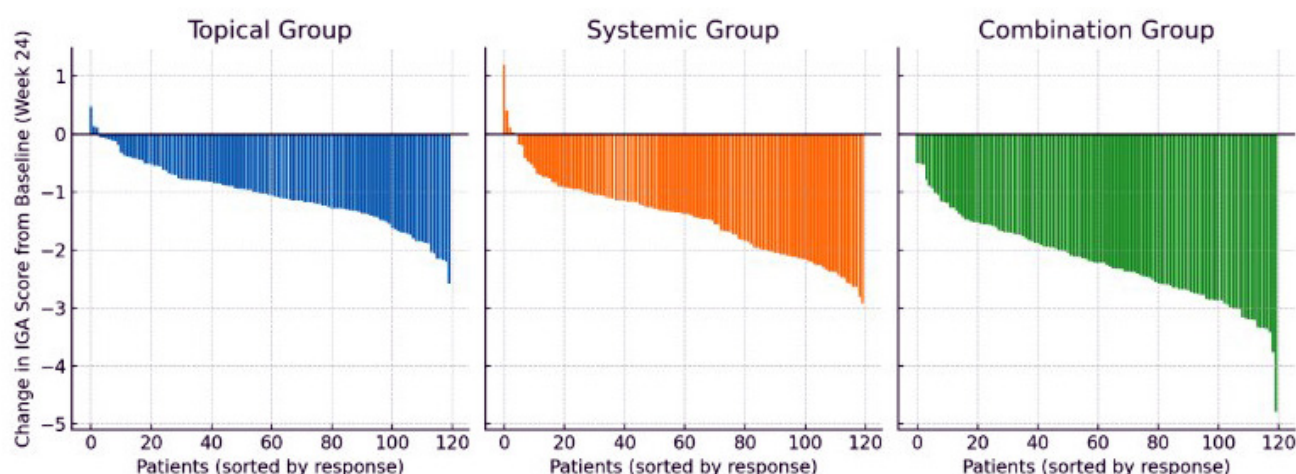
#### Quality of Life Outcomes

Significant improvements in DLQI and Acne-QoL scores were observed across all groups ( $p < 0.001$ ). Systemic and combination therapies resulted in earlier and greater QoL improvement, particularly by week 12.

A strong positive correlation was observed between reduction in inflammatory lesion counts and improvement in DLQI scores ( $r = 0.64$ ,  $p < 0.001$ ), indicating that clinical improvement translated directly into better psychosocial outcomes.



• Figure: Waterfall Plot of Individual IGA Response at Week 24



### Safety and Tolerability

Topical therapy was associated mainly with mild local irritation (dryness, erythema), whereas systemic therapy showed higher rates of gastrointestinal discomfort and photosensitivity. Combination therapy had the highest frequency of adverse events but few led to treatment discontinuation. No serious adverse events were reported.

### Discussion

This study provides robust comparative evidence on the efficacy and safety of topical versus systemic therapy in moderate-to-severe acne vulgaris. The findings demonstrate that systemic therapy, particularly when combined with topical agents, results in faster and greater clinical improvement compared to topical therapy alone.

The superior performance of systemic therapy in reducing inflammatory lesions aligns with its known anti-inflammatory and anti-*Cutibacterium acnes* mechanisms [11, 33]. The enhanced efficacy observed in the combination group supports the current guideline recommendation of multi-targeted therapy for moderate-to-severe acne [11, 12].

However, topical therapy alone still achieved meaningful clinical improvement and was associated with better tolerability, reinforcing its role as a suitable option for patients who cannot tolerate or prefer to avoid systemic agents. Importantly, quality-of-life improvements were seen in all groups, emphasizing that even moderate clinical improvement can significantly reduce psychosocial burden [8].

The correlation between clinical response and QoL improvement highlights the importance of early effective treatment to prevent long-term psychological consequences. These findings are consistent with previous studies demonstrating that acne-related QoL impairment can be comparable to chronic systemic diseases [8].

The study's strengths include its large sample size, randomized design, blinded outcome assessment, and incorporation of validated patient-reported outcome measures. Limitations include its single-center setting and lack of long-term relapse assessment.

## Conclusion

Systemic therapy offers superior short-term efficacy in moderate-to-severe acne vulgaris, while topical therapy provides a safer alternative with fewer systemic adverse effects. Combination therapy yields the most rapid and sustained improvement. Treatment decisions should be individualized, balancing disease severity, patient preference, tolerability, and psychosocial impact.

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