

# Efficacy of combination of topical 5% dapson plus oral doxycycline versus topical adapalene plus oral doxycycline in the treatment of moderate acne vulgaris

Zakir Ullah Khan<sup>1\*</sup>, Ziaullah Khan<sup>1</sup>, Hashim Khan<sup>2</sup>, Haya Sultan<sup>1</sup>, Khizar Hayat<sup>1</sup>, Maisan Bibi<sup>1</sup>

<sup>1</sup>Department of Dermatology, MTI-Hayatabad Medical Complex Peshawar.

<sup>2</sup>Department of Dermatology, Naseerullah Khan Babar Memorial Hospital, Peshawar.

## Abstract

**Background** Acne vulgaris is one of the most prevalent dermatological conditions worldwide, particularly affecting adolescents and young adults, with significant psychological and social impact. Topical and systemic agents are commonly combined to target multiple pathogenic pathways, yet comparative data on optimal regimens remain limited in the Pakistani population

**Objective** To compare the efficacy of combination of topical 5% dapson and oral Doxycycline versus topical adapalene and oral Doxycycline in the treatment of moderate acne vulgaris.

**Methods** This Quasi Experimental Study with two arms was conducted at the Department of Dermatology, MTI-Hayatabad Medical Complex (HMC), Peshawar, from 01 October 2023 to 01 April 2024. A total of 160 patients were enrolled, with 80 patients in each group. Group A received topical 5% dapson and oral Doxycycline, while Group B received topical adapalene and oral Doxycycline. Efficacy was evaluated using the Global Acne Grading System (GAGS) after 12 weeks of treatment.

**Results** In Group A, 27.5% showed excellent efficacy, while 26.25% in Group B showed similar results. Good and fair efficacy was observed in 25% of both groups. No significant difference in overall efficacy was observed between the groups ( $p=0.780$ ).

**Conclusion** Both treatment combinations are effective for moderate acne vulgaris, with no statistically significant difference in efficacy between the groups. Either treatment regimen can be considered for managing moderate acne.

**Keywords** Acne vulgaris; Dapson; Doxycycline.

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## Introduction

The common chronic inflammatory disease of the pilosebaceous units, acne is caused by abnormal follicular keratinization, inflammation, and proliferation of *C. acnes*.<sup>1</sup> Acne can be characterized by open and closed comedones, erythematous

papules, pustules, nodules, deep pustules, pseudo cysts, and in rare cases, scarring.<sup>2</sup>

It is estimated that over 85% of teenagers suffer from acne. Acne often begins during adolescence and gradually goes away by the time a person is 20 years old, while in rare instances, some people may still experience acne in their 40s and 50s.<sup>3</sup> Acne vulgaris can be treated with either a combination or a single treatment. Systemic therapy and topical application are two examples of different therapeutic techniques. The cornerstones of treatment in topical

## Address for correspondence

Dr. Zakir Ullah Khan,  
Department of Dermatology,  
MTI-Hayatabad Medical Complex Peshawar.  
Ph:+92313 8591234  
Email: zakir100khan@gmail.com

agents are retinoids, sulfone, salicylic acid antibiotics, and benzoyl peroxide. Tetracyclines, macrolides, clindamycin, and isotretinoin are examples of systemic therapy.<sup>4-6</sup> Since doxycycline is more lipophilic than its parent tetracycline, it can accumulate in the sebaceous gland, which is home to and the site of *C. acnes*'s proliferation. It inhibits bacterial protein synthesis, binds reversibly to the 30S component of ribosomes, and has antibacterial and anti-inflammatory properties.<sup>3,4</sup> A novel synthetic topical retinoid of the third generation, adapalene is made from naphthoic acid. Third-generation retinoid adapalene has anti-inflammatory, comedolytic, and sebum-reducing properties.<sup>7</sup> Dapsone is a sulfone that has antibacterial and anti-inflammatory qualities. 5% dapsone gel was approved by the FDA in 2008 for clinical indications including acne.<sup>8</sup>

An international study was conducted in year 2019 in which combination of oral Doxycycline and topical application of adapalene was effective in 67% of patients.<sup>9</sup> An international study conducted in Iran reported 85% improvement in acne lesions with the use of oral Doxycycline along with topical 5% dapsone gel.<sup>10</sup>

Despite growing evidence supporting each agent individually, there is a critical lack of direct head-to-head comparative data between topical dapsone and topical adapalene when combined with oral doxycycline-particularly within the Pakistani population, where prescribing practices, patient demographics, and treatment access differ from Western settings. This gap in local evidence limits the ability of clinicians to make evidence-based treatment choices. The purpose of this study was therefore to directly compare the efficacy of these two combination regimens in patients with moderate acne vulgaris presenting to a tertiary care centre in Peshawar. To the best of we aware, no local research has been done on the subject, therefore this study will assist in figuring out the most effective local treatment for moderate acne. The study's findings will be disseminated to nearby dermatologists in order to develop guidelines, which will aid in the

improved treatment of moderate acne in our community.

## **Methods**

Over the course of six months, from October 1, 2023, to April 1, 2024, the Dermatology Unit, Hayatabad Medical Complex, Peshawar conducted this quasi-experimental study with two parallel arms. A non-probability consecutive sampling strategy was used to enrol 160 patients with a diagnosis of moderate acne vulgaris. Acne severity and diagnosis were assessed clinically and scored using the Global Acne Grading System (GAGS). A score of 19 to 30 on the GAGS was considered moderate acne. Comedones (small, flesh-colored, white, or dark bumps), papules (solid, raised lesions <1 cm), pustules (pus-filled, inflamed lesions), and no more than one nodule (elevated lesion >0.5 cm in diameter) were clinical characteristics of moderate acne.

Based on an expected efficacy of 85% for oral doxycycline plus topical dapsone and 67% for oral doxycycline plus topical adapalene, at a 95% confidence interval and 80% power, the sample size was determined using the WHO sample size calculator. Participants were patients with moderate acne vulgaris, ages 14 to 30, of both sexes, who had not taken any topical or systemic anti-acne medication during the previous four weeks. Patients with severe nodulocystic acne, acne fulminans, secondary acne, acne conglobata, pregnancy, lactation, or a history of doxycycline, dapsone, or adapalene hypersensitivity were not included.

After taking written informed consent from all participants, and following approval from the Institutional Review Board (IRB) of Hayatabad Medical Complex, Peshawar (Reference No. 1160 23.01.2023), we recorded demographic data along with clinical history and GAGS score. Patients were assigned to one of two groups using a systematic alternating allocation method (odd-numbered patients to Group A, even-numbered to Group B) based on order of clinic attendance. As this was a

quasi-experimental study, formal randomization was not performed; this represents a study limitation. Group A were given oral doxycycline 100mg once daily with adjuvant topical 5% dapson gel at night time while group B were given oral doxycycline 100 mg once daily in combination with topical adapalene gel applied nightly. All were then followed for period of 12 weeks with four weekly visits. On every visit after 4 week, GAGS score was calculated. On the basis of this treatment response was calculated each time using the following formula: Percentage decrease = (Baseline score – Post-treatment score/ Baseline score) × 100. Treatment efficacy was stratified on the basis of reduction in acne based on the above formula as such: Excellent (>75% reduction), Good (50–74%), Fair (25–49%), and Poor (<25%).

Data analysis was done using IBM SPSS software, version 23. Apart from descriptive statistics, the Chi-square test was used to compare categorical variables, including treatment efficacy categories and demographic characteristics between the two groups, while the Mann-Whitney U test was applied to compare non-normally distributed continuous variables such as GAGS scores. A p-value of ≤0.05 was considered statistically significant for all analyses.

### Result

A total of 160 patients were enrolled in the study, with 80 participants in each treatment arm. The mean age of the study population was 22.75±4.03 years. Group A had a mean age of 22.50±3.95 years, while Group B had a mean age of 23.00±4.10 years. Baseline characteristics are described in **Table 1**.

**Table 1** Baseline characteristics of study groups (n=160).

Characteristics	Group A (n=80)	Group B (n=80)	Total (n=160)	p-value
<b>Age Group</b>				0.820
Second Decade	37 (46.25%)	38 (47.5%)	75 (46.87%)	
Third Decade	43 (53.75%)	42 (52.5%)	85 (53.13%)	
<b>Gender</b>				0.680
Male	42 (52.5%)	44 (55.0%)	86 (53.75%)	
Female	38 (47.5%)	36 (45.0%)	74 (46.25%)	

**Table 2** Comparison of GAGS among two groups by Mann Whitney U test.

Group	Pre-Treatment GAGS	Post-Treatment GAGS	Mean % GAGS Reduction	P-value
Group A	24.50±3.35	13.50±2.95	44.90%	0.780
Group B	25.00±3.20	14.00±3.00	44.00%	

The baseline mean Global Acne Grading System (GAGS) was compared in **Table 2**. Mean percentage reduction was noted to be 44.90% in Group A and 44.00% in Group B with p value of 0.780.

No significant post treatment efficacy among treatment group, age and gender were noted with p-value of 0.780, 0.93, 0.73, 0.92, 0.87 respectively as shown in **Table 3**.

### Discussion

This quasi-experimental study compared the efficacy of two combination treatment regimens - topical 5% dapson plus oral doxycycline versus topical adapalene plus oral doxycycline - in patients with moderate acne vulgaris. Given the limited head-to-head comparative data for these specific combinations in the local Pakistani population, these findings contribute valuable clinical evidence to guide treatment decisions in this setting.<sup>11</sup>

**Table 3** Post-Treatment Efficacy Comparison by Treatment Group, Age Group, and Gender (n = 160).

Category	Subgroup	Excellent	Good	Fair	Poor	Total (n)	p-value
Treatment Group	Group A (n = 80)	22 (27.5%)	21 (26.25%)	20 (25.0%)	17 (21.25%)	80	0.780
	Group B (n = 80)	21 (26.25%)	17 (21.25%)	20 (25.0%)	22 (27.5%)	80	
	Total	43 (26.88%)	38 (23.75%)	40 (25.0%)	39 (24.38%)	160	
Age Group	Second Decade	23 (29.5%)	18 (23.1%)	18 (23.1%)	19 (24.4%)	75	0.930
	Third Decade	20 (24.4%)	20 (24.4%)	22 (26.8%)	20 (24.4%)	85	0.730
Gender	Male	23 (26.7%)	20 (23.3%)	22 (25.6%)	21 (24.4%)	86	0.920
	Female	20 (27.0%)	18 (24.3%)	18 (24.3%)	18 (24.3%)	74	0.870

Chi Square or Fishers exact test was used for comparison.

With a mean age of  $22.75 \pm 4.03$  years, the majority of participants were in their third decade of life, which is similar to the results of Dhaher *et al*; who found that the mean age was  $20.9 \pm 3.4$  years.<sup>12</sup> The high incidence of acne vulgaris in adolescence and early adulthood is probably the cause of this resemblance. Males marginally outnumbered females among the recruited patients, resulting in a male-to-female ratio of 1.16:1, which is in line with Singh *et al*'s findings, which indicated a ratio of 2.4:1.<sup>13</sup> Males' greater androgen secretion, which increases sebum production and leads to more frequent and severe acne lesions, may be the cause of this pattern. On the other hand, Dhaher *et al*. found that the prevalence was higher in women, with a male-to-female ratio of 0.89:1.<sup>11</sup> This is probably because women are more inclined to seek medical attention because they are more concerned about their appearance.

In accordance with the moderate acne severity documented in the study by Darjani *et al*; which had a mean GAGS score of 23.75,<sup>10</sup> the baseline Global Acne Grading System (GAGS) scores for Group A and Group B were 24.50 and 25.00, respectively. Since both trials limited participation to patients with moderate acne vulgaris, this alignment might be the result of identical inclusion criteria. Significant gains in GAGS scores were shown by both treatment plans: Group A's increased from  $24.50 \pm 3.35$  to  $13.50 \pm 2.95$ , while Group B's increased from  $25.00 \pm 3.20$  to  $14.00 \pm 3.00$ . Although direct comparisons between these two specific drug combinations are lacking in existing literature, studies evaluating oral doxycycline with either topical dapsone or adapalene have independently demonstrated significant efficacy. The current study's observed decrease in GAGS scores is consistent with earlier findings demonstrating the efficacy of both combinations in treating moderate acne vulgaris.

There was no statistically significant difference ( $p=0.780$ ) between the two groups' excellent, good, fair, and poor reactions to the category therapy, which were 27.5% vs. 26.25%, 26.25% vs. 21.25%,

25.0% vs. 25.0%, and 21.25% vs. 27.5%, respectively. Using such stratified response categories, no previous study has directly compared the effectiveness of these two medication combinations. However, Kircik *et al*. observed positive outcomes utilizing oral doxycycline with topical dapsone 5% gel in moderate-to-severe cases,<sup>15</sup> and Zaenglein *et al*. showed the advantage of combining oral doxycycline with topical retinoids to address both inflammatory and non-inflammatory lesions.<sup>14</sup>

However, neither study used stratified response categories to define efficacy. The strong anti-inflammatory qualities of dapsone and adapalene, along with their corresponding antibacterial and retinoid-mediated modes of action, may be responsible for the similar outcomes seen in this investigation. Therefore, for moderate acne vulgaris, either topical medication plus oral doxycycline can be regarded as an efficient and well-tolerated treatment plan.

Both treatment groups shown comparable efficacy across age strata in terms of age-based response. Groups A and B responded well in 32.4% vs. 28.9%, well in 21.6% vs. 21.0%, fairly in 21.6% vs. 23.6%, and poorly in 24.3% vs. 26.3% over the second decade, respectively ( $p=0.930$ ). The similar values for the third decade were 20.0% vs. 28.6% for bad responses, 27.5% vs. 21.4% for good, 27.5% vs. 26.2% for fair, and 23.2% vs. 23.8% for exceptional ( $p=0.730$ ). Our results are consistent with those of Bhate and Williams, who found that treatment responses among adults and adolescents were similar, despite the fact that few studies have examined age-related treatment outcomes using such thorough stratification.<sup>16</sup> This may be due to the uniform pharmacodynamic effects of topical agents across age groups, particularly when patients with similar acne severity, such as moderate acne, are selected for treatment.

Furthermore, no significant gender-based differences in treatment efficacy were observed (0.920 and 0.870, respectively). It aligns with the findings of

study by Eichenfield *et al*; who reported no substantial gender differences in acne treatment response.<sup>17</sup> Contrastly, Zaenglein *et al*. reported that due to hormonal differences between male and female, with elevated levels of androgen in female has higher chances of failure of treatment.<sup>18</sup>

## Conclusion

This study demonstrated that there was no significant difference between both oral doxycycline combined with topical dapson, and oral doxycycline combined with topical adapalene in effectively treating the patients of moderate acne vulgaris (p-value=0.780). However, these findings should be interpreted in the context of the study's design limitations, including its quasi-experimental non-randomized nature, consecutive sampling, and single-centre setting. Future randomized controlled trials with longer follow-up periods are recommended to validate these results.

**Limitations** Our study is subjected to few limitations worth mentioning. First selection bias might be present as the study was quasi-experimental and non-randomized one. Generalizability is restricted when consecutive sampling is used. When evaluating long-term results, the 12-week follow-up is comparatively brief. There was no objective way to quantify topical therapy adherence. Furthermore, the application is limited to moderate acne only due to the exclusion of severe acne instances.

**Declaration of patient consent** Authors certify that they have obtained all appropriate patient consent.

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**Conflict of interest** No conflict of interest.

## Author's contribution

**YUK:** Substantial contribution to study design, manuscript writing.

**YK:** Substantial contribution to acquisition of data, manuscript writing.

**HK,HS:** Substantial contribution to data analysis and interpretation of data, writing.

**KH:** Substantial contribution to data analysis and interpretation of data, critical review of the manuscript.

**MQ:** Contribution to concept, study design, critical review of the manuscript.

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