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COMPARATIVE EFFICACY OF ORAL DOXYCYCLINE AND MONTELUKAST IN TREATMENT OF MILD TO MODERATE INFLAMMATORY ACNE

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ABSTRACT

Objective: To compare the mean change in acne severity index with oral doxycycline and oral montelukast in treatment of mild to moderate inflammatory acne.

Methods: This quasi-experimental study was instituted at a dermatology department of Combined Military Hospital (CMH) ,Abbottabad, KPK from July 2025 to October 2025, 58 patients with moderate acne were initially enrolled. The study sample was divided into two groups, 28 patients in the Montelukast group and 30 in the Doxycycline group. Baseline characteristics, including age, gender, and Global Acne Grading System (GAGS) scores, were comparable between groups. Patients received either oral Doxycycline or Montelukast for 8 weeks, and outcomes were assessed in terms of changes in acne severity (GAGS), acne-related quality of life (AQL), and treatment-related adverse events.

Results: Both therapies effectively alleviated acne symptoms while contributing to improvements in quality of life. The Doxycycline group showed a greater reduction in GAGS scores (mean change 4.5 ± 1.2) compared with the Montelukast group (1.8 ± 0.6, $p < 0.001$). Quality of life improved in both groups, with the Doxycycline group showing a more substantial decrease in AQL scores (18.4 ± 3.1 to 14.4 ± 2.8, $p < 0.001$) than the Montelukast group (19.1 ± 3.0 to 15.2 ± 3.3, $p = 0.04$). Adverse events were mild, including gastrointestinal upset and headache in Doxycycline group .

Conclusion: Doxycycline demonstrated superior efficacy in reducing acne severity and improving quality of life compared with Montelukast. However, considerations such as antibiotic resistance, side effects, and patient preference should guide treatment selection. Montelukast, with a favorable safety profile, may serve as a useful adjunct or alternative therapy.

Keywords: Acne vulgaris, Montelukast, Doxycycline, Systemic therapy, Anti-inflammatory treatment

INTRODUCTION

Inflammatory acne vulgaris poses a momentous global dermatological burden as it affects over 10% of global population [1]. Acne vulgaris is marked by insistent scarring and keen psychological impacts which impair quality of life [2]. Systemic treatment modalities for inflammatory acne vulgaris predominantly include oral antibiotics and hormonal therapy [3]. For severe or refractory cases oral isotretinoin is used [4]. Doxycycline is widely utilized owing to its well-recognized efficacy, accessibility, and relatively low cost. It acts not only by inhibiting bacterial proliferation but also by tempering inflammatory activity within the pilosebaceous unit [5]. Nonetheless, the sustained use of oral antibiotics is increasingly encumbered by concerns related to antimicrobial resistance, drug-related adverse effects, and the broader implications of prolonged systemic exposure [6,7]. These drawbacks have driven enquiry into alternative agents with anti-inflammatory potential [8]. Montelukast, a cysteinyl leukotriene receptor antagonist, has emerged as a reasonable alternative. Considering that it may mitigate inflammatory processes involved in acne pathogenesis. By targeting leukotriene-mediated inflammation, it may furnish clinical benefit without amplifying the resistance concerns associated with chronic tetracycline therapy [9,10]. Conversely, montelukast rarely causes serious side effects in the body, although some cases of neuropsychiatric events which includes mood changes, insomnia and suicidal thoughts have led to question its safety in particular groups [11]. Thus, the present study was designed to compare the efficacy of oral doxycycline and oral montelukast in the treatment of mild to moderate inflammatory acne. The study objective was to compare

the mean change in acne severity index with oral doxycycline and oral montelukast in treatment of mild to moderate inflammatory acne.

METHODOLOGY

This quasi-experimental study was instituted at a dermatology department of Combined Military Hospital (CMH) ,Abbottabad, KPK from July 2025 to October 2025. The target population was male and female patients aged 15 to 35 years presenting with mild to moderate inflammatory acne to the respective hospital department. Patients with a Global Acne Grading System (GAGS) score of 1 to 30, having papules and pustules with or without comedones and no more than one nodule, were eligible for inclusion. Only those with disease duration of more than three months were be enrolled.

Patients were excluded due to systemic steroids, retinoids, or immunosuppressants used for acne during the preceding four weeks. Those with known hypersensitivity or any contraindication to doxycycline or montelukast were also omitted. Additionally, patients with active psychiatric illness, neuropsychiatric disorders, hepatic impairment, or renal impairment were not included. Females with severe acne secondary to polycystic ovary syndrome, pregnant and lactating were excluded. The sample size for this study was determined using the WHO sample size calculator. The calculation was based on the data from a previous local study by Aslam et al. (2020), which reported the following results for acne severity index (ASI) changes: in the doxycycline group (Group A), the mean change in ASI was 5.45 ± 1.29, and in the montelukast group (Group B), the mean change in ASI was 1.80 ± 0.59. The mean difference in acne severity change between the two groups was calculated as 3.65 (5.45 - 1.80). The sample size per group was estimated to be 28 participants. However, to account potential dropouts at 10% rate, the sample size was increased to 30 participants per group [12].

Participants were assigned to two treatment groups (group A and B). The group A received oral doxycycline (100 mg daily) for 8 weeks, with regular follow-ups to monitor for any adverse effects. The second group received oral montelukast (10 mg daily) for the same period. The study assessed change in acne severity as the primary outcome, using the GAGS at baseline, 4 weeks, and 12 weeks to evaluate the number and type of lacerations on the face, back and chest. All patients were advised to follow a standard acne care regimen including gentle face washing twice daily. In addition, patients were advice to avoid any over-the-counter acne products. No topical or systemic acne treatments other than the assigned intervention were permitted.

Secondary outcomes included patient-reported outcomes, using the validated Acne Quality of Life (AQL) questionnaire to assess the psychological impact of acne at baseline and after 8 weeks. The question has 12 questions regarding psychological distress, social and daily challenges due to acne. The questions are rated on four point Likert scale, total score ranging between 0 to 27. Adverse effects such as gastrointestinal upset or headache were also documented at each follow-up visit [13].

Data was collected at baseline, at 4-week follow-ups, and at the final 12-week visit. Statistical analyses included descriptive statistics to summarize demographic data and changes in acne severity. The primary comparative analysis used a paired t-test or Mann-Whitney U test to assess the changes in acne severity between the two treatment groups. Secondary outcomes, including changes in inflammatory markers and quality of life, were analyzed using appropriate statistical tests based on data distribution. The incidence of adverse events was compared between groups using chi-squared tests.

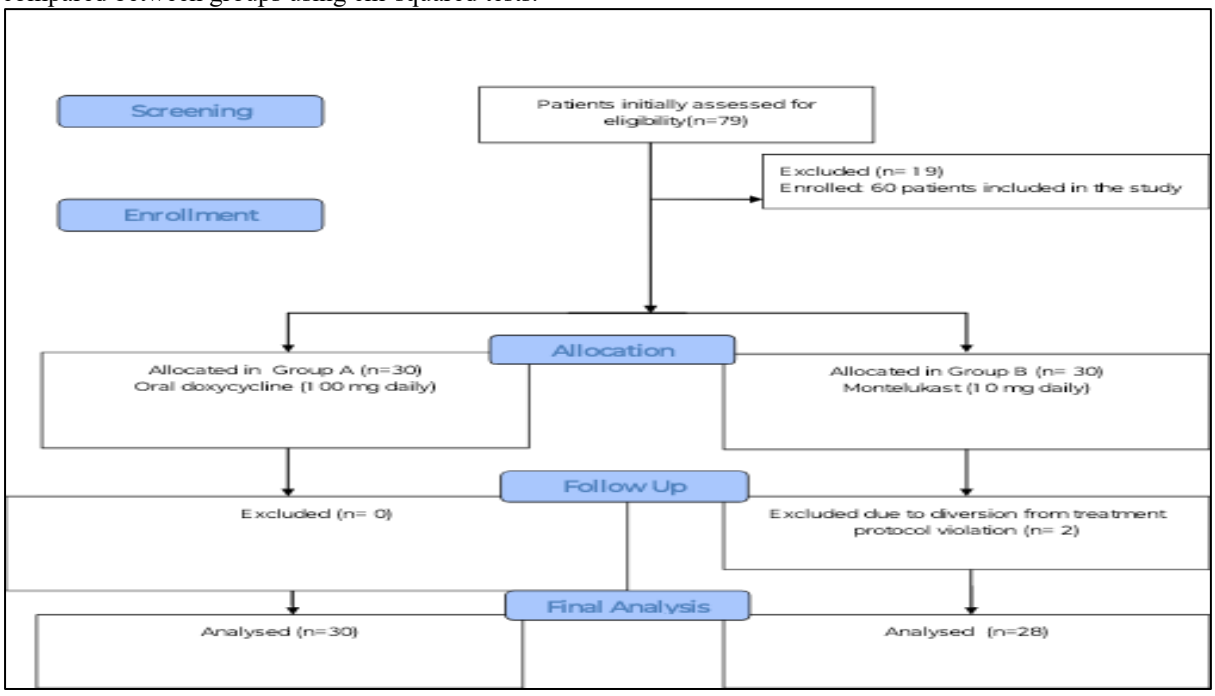

Figure 1: Patient recruitment flowchart

RESULTS

A total of 60 patients were initially enrolled in the study. Two patients from the montelukast group were excluded from the final analysis due to the use of topical acne treatments. So final analysis was conducted on 28 participants remaining in the montelukast group and 30 participants in the doxycycline group. The sociodemographic characteristics of the participants in both groups are summarized in Table I. The groups were well-matched in terms of baseline characteristics.

Table 1: Comparison of Baseline characteristics of the study Groups (N=58)

Characteristic	Doxycycline Group (n=30)	Montelukast Group (n=28)	p-value
Age (years)	28.3± 4.1	26.9 ± 3.9	0.07
Gender			
Male	14 (46.7%)	15 (53.6%)	1.00
Female	16 (53.3%)	13 (46.4%)	1.00
Baseline Acne Severity (GAGS)	25.8 ± 1.9	24.9 ± 2.1	0.45

The Doxycycline group (n=30) demonstrated a significant reduction in acne severity, with a post-treatment GAGS score of 21.3 ± 1.5 and a mean change of 4.5 ± 1.2 from baseline ($p < 0.001$). The Montelukast group (n=28) showed a more modest reduction in acne severity, with a post-treatment GAGS score of 23.1 ± 2.4 and a mean change of 1.8 ± 0.6 ($p < 0.001$). When comparing the two groups, the Doxycycline group showed a more substantial reduction in acne severity than the Montelukast group.

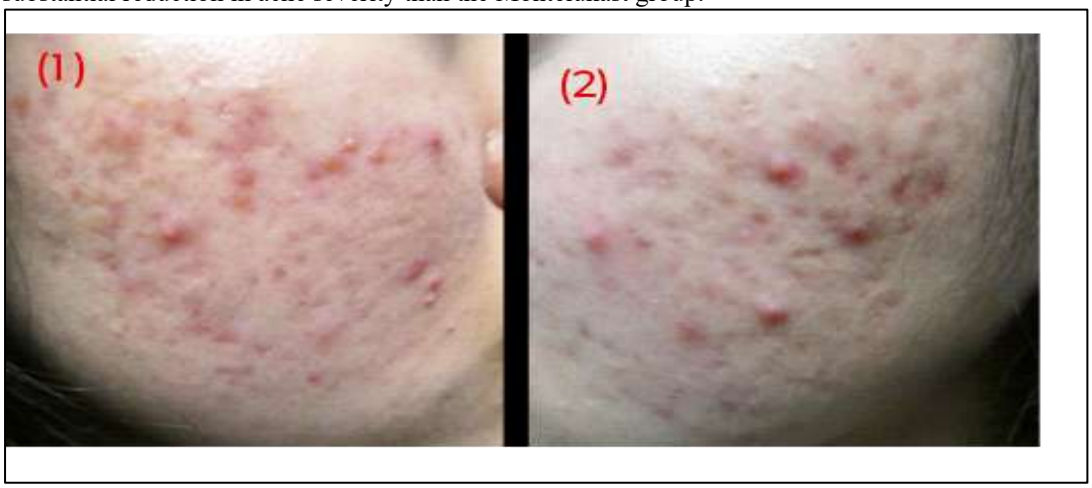

Figure 2: Effect of montelukast (1) Before treatment. (2)

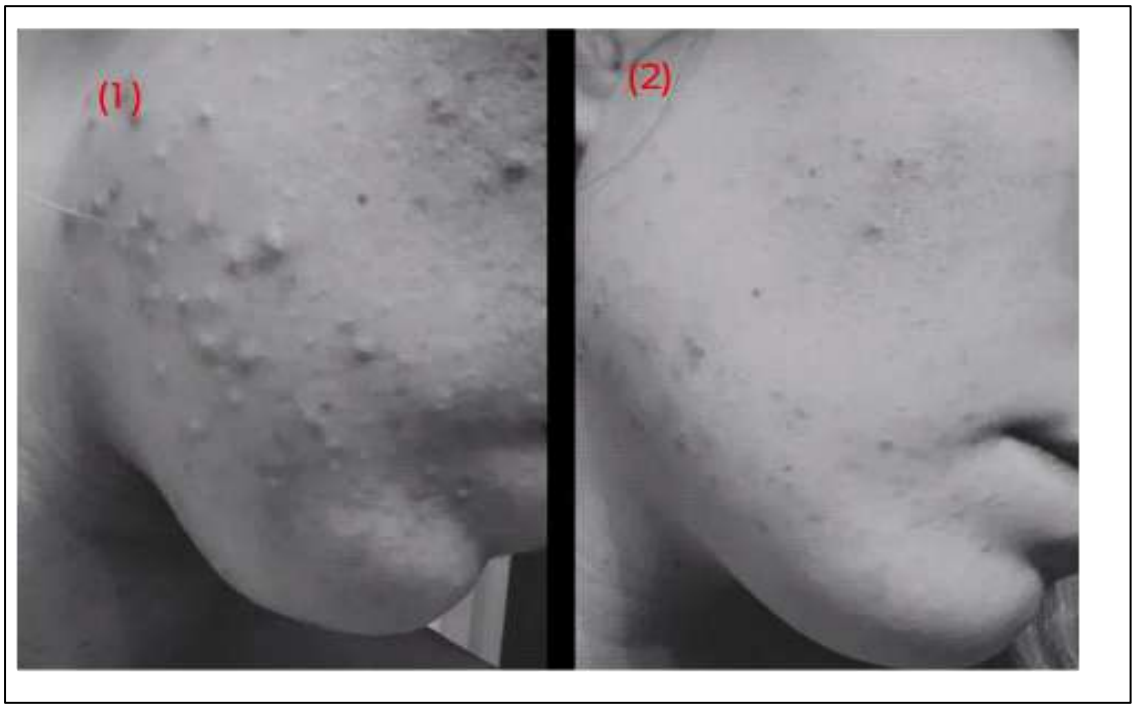

Figure 3: Effect of Doxycycline treatment (1) Before treatment. (2) After treatment

Table 2: Comparison of change in Acne severity between groups

	Post-Treatment Acne Severity (GAGS)	Change in Acne Severity (GAGS)	p-value
Doxycycline (n=30)	21.3 ± 1.5	4.5 ± 1.2	<0.001
Montelukast (n=28)	23.1 ± 2.4	1.8 ± 0.6	<0.001
Doxycycline vs. Montelukast			<0.001

The figure below shows the baseline and 8-week AQL scores for both treatment groups. The Doxycycline group (n=30) demonstrated a significant improvement in quality of life, with the baseline AQL score of 18.4 ± 3.1 significantly decreasing to 14.4 ± 2.8 after 8 weeks ($p < 0.001$). Similarly, the Montelukast group (n=28) showed a reduction in the AQL score from 19.1 ± 3.0 at baseline to 15.2 ± 3.3 after 8 weeks ($p = 0.04$).

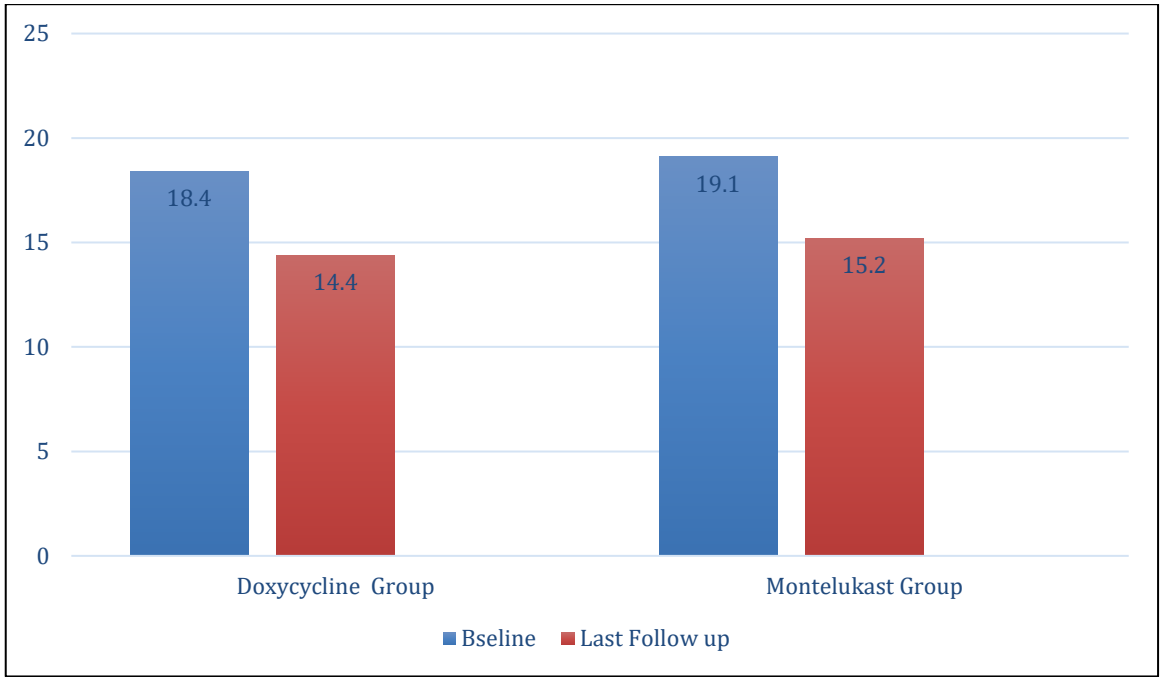

Figure 4: Comparison of mean AQL scores at baseline and final follow up between groups

The Doxycycline group had 5 cases of gastrointestinal upset (16.7%), while the Montelukast group had only one case. The difference between the two groups was not statistically significant ($p = 0.18$). Likewise, headache was reported in 2 participants (6.7%) in the Doxycycline group. The difference was not statistically significant ($p = 0.43$).

Table 3: Comparison of adverse effect during treatment among study groups

Variable	Doxycycline Group (n=30)	Montelukast Group (n=28)	p-value
Gastrointestinal Upset	5 (16.7%)	1 (3.5%)	0.18
Headache	2 (6.7%)	-	0.43

DISCUSSIONS

The objective of this analysis was to compare the mean change in acne severity index with oral doxycycline and oral montelukast in treatment of mild to moderate inflammatory acne. The analysis also assessed the safety profiles of doxycycline versus montelukast in treating acne vulgaris, hypothesizing that montelukast would demonstrate superior tolerability. The Doxycycline group demonstrated a significant reduction in acne severity. In contrast, the Montelukast group showed a more modest reduction in acne severity. Both treatments were effective in reducing acne severity, but Doxycycline showed a more significant improvement in acne severity compared to Montelukast. These findings align with previous studies, which have also explored the role of Montelukast in acne treatment [14,15,16]. For example, a study by Negin Fazelzadeh Haghighi et al. (2022) demonstrated that Montelukast, when used alongside doxycycline, led to a reduction in inflammatory lesions and improved the Investigator Global Assessment (IGA) and GAGS scores. Their results indicated a more significant reduction in inflammatory lesions and IGA scores in the Montelukast group ($p = 0.018$ and 0.045, respectively) compared to the placebo group. This suggests that Montelukast may have a potential role as an adjuvant therapy, particularly for inflammatory lesions in acne [14].

Other studies have explored the role of Montelukast in acne treatment. Rokni et al. conducted a comparison of treatment with oral montelukast and oral finasteride. Topical clindamycin 2% was administered to both groups simultaneously. The study demonstrated that both treatment methods were effective, with finasteride

demonstrating a superior outcome in comparison to montelukast [15]. Consistently, Bourget et al. (2021) observed a reduction in acne severity and improvement in quality of life among patients treated with Montelukast, particularly for those with moderate to severe acne vulgaris. In spite of the encouraging results reported in some studies regarding the anti-inflammatory role of Montelukast in acne management. Its overall therapeutic effectiveness compared with conventional systemic treatments remains debatable [17]. In line with this context, the present study specifically aimed to compare the efficacy and tolerability of Montelukast and Doxycycline in patients with moderate acne. Our findings demonstrated that although both treatments produced improvement in acne severity, the reduction in acne scores was significantly greater in the Doxycycline group, indicating a comparatively stronger therapeutic effect. This difference may be attributed to the broader mechanism of action of doxycycline, which targets both the bacterial component and inflammatory pathways involved in acne pathogenesis, whereas montelukast primarily acts through leukotriene-mediated anti-inflammatory pathways [9,18]. Consequently, while Montelukast may provide clinical benefit, particularly in inflammatory lesions, its role as a primary therapeutic option appears limited when compared with established antibiotic therapy.

Another important finding of our study was that that the doxycycline cohort experienced mild gastrointestinal distress and headache, while montelukast showed no significant adverse events, highlighting its superior safety profile. This aligns with literature on tetracyclines reporting gastrointestinal issues, photosensitivity, and discontinuation risks [19,20]. Antibiotics more frequently provoke musculoskeletal and CNS effects than non-antibiotic options [21], reinforcing montelukast's tolerability edge, though it exhibited less potent anti-inflammatory effects than doxycycline for rapid improvement.

While systemic antibiotics like doxycycline provide rapid reduction in inflammatory lesions, the escalating concern regarding antimicrobial resistance necessitates the adoption of agents with alternative mechanisms of action [22]. The observed shift toward non-antibiotic modalities mirrors broader clinical trends that prioritize the reduction of microbial resistance in chronic skin conditions [7]. Consistent with this, montelukast demonstrated a favorable safety profile with no treatment-associated adverse events reported in the current study, contrasting with the gastrointestinal side effects observed in the doxycycline group. However, clinicians must remain vigilant regarding the potential for minimal but significant neuropsychiatric adverse effects, such as mood alterations, which have been noted in broader safety evaluations of this medication [23]. Nonetheless, given the increasing clinical emphasis on antimicrobial stewardship, prioritizing such non-antibiotic therapies remains a critical strategy to prevent the perturbation of the skin microbiome and the emergence of resistant strains.

CONCLUSIONS

Both Montelukast and Doxycycline treatments significantly reduced acne severity and improved quality of life in mild to moderate acne patients. Still, Doxycycline demonstrated a greater reduction in GAGS scores and more pronounced improvement in patient-reported outcomes compared with Montelukast ($p < 0.001$). Both treatments were generally well tolerated, with only mild gastrointestinal upset and headache reported.

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