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Original Research Article

COMPARATIVE STUDY OF EFFICACY OF LOW-DOSE CONTINUOUS AND LOW-DOSE INTERMITTENT ORAL ISOTRETINOIN THERAPY IN MODERATE ACNE VULGARIS

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ABSTRACT

Background: *Acne vulgaris is a common dermatological condition that significantly affects quality of life. Isotretinoin is the most effective treatment for moderate-to-severe cases. Still, concerns regarding dosing strategies and adverse effects have led to investigations into alternative regimens such as low-dose continuous and intermittent therapies.* ***Objective:*** *To compare the efficacy of low-dose continuous and low-dose intermittent oral isotretinoin therapy in patients with moderate acne vulgaris.* ***Study Design:*** *Quasi-experimental design.* ***Setting:*** *Department of Dermatology, Combined Military Hospital, Nowshera, Pakistan.* ***Duration of Study:*** *08-February-2025 to 08-June-2025.* ***Methods:*** *A total of 112 participants aged 18–60 years with clinically diagnosed moderate acne vulgaris were enrolled and equally allocated into two groups (n=56 each). Group A received continuous oral isotretinoin (20 mg once daily for 2 months), while Group B received intermittent oral isotretinoin (20 mg once daily for 1 week per 4-week cycle over 2 months). Efficacy was defined as at least a 10-point reduction in Global Acne Grading System (GAGS) score from baseline to 2 months. An independent t-test was applied to compare pre- and post-treatment GAGS scores, with a significance threshold set at $p \leq 0.05$.* ***Results:*** *The mean age of participants was 30.71 ± 10.13 years in Group A and 29.43 ± 8.55 years in Group B. Following treatment, mean GAGS scores were 10.43 ± 5.53 in Group A and 8.75 ± 5.99 in Group B. No statistically significant difference was observed between the groups ($p = 0.12$). Both regimens demonstrated clinically meaningful improvement.* ***Conclusion:*** *Low-dose continuous and low-dose intermittent oral isotretinoin therapies are similarly effective for the management of moderate acne vulgaris. Both regimens can be considered safe and effective alternatives in clinical practice.*

Keywords: Moderate Acne Vulgaris, Oral Isotretinoin, Low-Dose Therapy, Continuous Regimen, Intermittent Regimen, Treatment Efficacy

INTRODUCTION

Acne vulgaris (AV) is a prominent inflammatory condition affecting the pilosebaceous unit, characterised by chronic progression. The pathological process of AV includes the interplay of different variables that culminate in the development of its central lesion (1-3). Lesions tend to appear on the face, upper back, and chest. Acne manifests in various forms, including occupational acne, acne fulminans, excoriated acne, and drug-induced acne, which can result from specific materials. These variants exhibit resemblance to AV both clinically and histologically; however, differences in clinical presentation, severity, and accompanying symptoms may differentiate them (4). AV frequently occurs in adolescents; however, it isn't limited to that demographic and affects individuals across various ages. This condition demonstrates a spectrum of severity, from mild manifestations with minimal comedones to severe types marked by noteworthy inflammatory responses, which may result in hyperpigmentation and negative emotional consequences (5-8). About 70.2% of respondents have either current or past experiences with acne, primarily affecting the facial area (92%). The prevalence of AV was greater among individuals aged 23-25 years, especially among females (9).

Isotretinoin is an oral medication that focuses on sebaceous glands, usually indicated for the treatment of severe acne (10). American Academy of Dermatology standards recommend isotretinoin to people with severe acne or those not responding to conventional treatments, such as both oral and topical therapies. Individuals with acne who face significant emotional distress or scarring ought to be evaluated as potential candidates for isotretinoin treatment. The recommendations are conventional daily administration of isotretinoin to people with severe acne, as compared to intermittent dosing. Both standard isotretinoin and low-dose isotretinoin are possible choices (11). Low-dose oral-isotretinoin shows superior bioavailability when compared to conventional isotretinoin, attributable to a pre-solubilized lipid framework (12).

Traditional high-dose oral isotretinoin therapy has demonstrated significant efficacy in treating severe acne, but potential adverse effects and concerns about long-term safety often limit its use. Since no local data is available on this subject, this study aims to compare the efficacy of low-dose continuous and low-dose intermittent oral isotretinoin therapy in patients with moderate AV at our hospital. The findings of this study will be helpful for our clinicians to offer more flexible, patient-centered treatment options and contribute to more personalized management strategies for AV.

METHODOLOGY

This study employed a quasi-experimental design, conducted at the Department of Dermatology, Combined Military Hospital, Nowshera, from 08 February 2025 to 08 June 2025, following ethical approval from the hospital. One hundred and twelve participants were enrolled; the sample was calculated using the WHO sample size calculator. This calculation was based on prior findings where the mean improvement in global acne grading scores was reported as 2.04 ± 0.28 (13) for continuous therapy and 1.88 ± 0.32 (13) for intermittent treatment with a power of 80% and a confidence level of 95%. Consecutive non-probability sampling was utilized.

Patients aged 18 to 60 years diagnosed with moderate acne vulgaris, which was characterized by the presence of Comedones (10 to 30 open and closed comedones combined), Papules (10 to 20 small, raised, red

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bumps), Pustules (5 to 15 papules with a visible pus-filled center), Nodules (typically less than five i.e larger, deep-seated lesions) and Cysts (typically less than five i.e deep, inflamed, pus-filled lesions). Exclusion standards comprised individuals with diabetes mellitus, known allergies to isotretinoin, abnormal lipid profiles, or hepatic and renal dysfunction. Each participant gave their consent.

The intervention involved two distinct regimens. Group A (n = 56) received low-dose continuous oral isotretinoin therapy consisting of 20 mg once daily for two months. Group B (n = 56) was administered low-dose intermittent treatment with 20 mg once daily for one week out of every four weeks over the same duration. Efficacy was assessed using the Global Acne Grading System (GAGS) score, with a reduction of at least 10 points after two months considered indicative of improvement. All evaluations were conducted by a dermatologist with a minimum of five years of post-fellowship experience to ensure consistency and accuracy. Data collection was performed using a pre-designed structured proforma, which documented baseline and post-treatment GAGS scores alongside other relevant variables.

SPS 23 was used for analysis. Age, BMI, duration of acne, baseline, and post-treatment GAG score were evaluated using mean and standard deviation. Gender, location of acne, socioeconomic status, residence, education, and occupation were presented as frequencies and percentages. An independent sample t-test was used to assess the post-treatment GAG score between both groups, and the P value was kept statistically significant at ≤ 0.05. Age and gender were stratified with GAG score in both groups, using the Independent sample t-test, keeping the P value notable at ≤ 0.05.

RESULTS

In our study, Group A, which received continuous oral isotretinoin, had a mean age of 30.71 ± 10.13 years, whereas Group B, the intermittent therapy group, had a mean age of 29.43 ± 8.55 years. The mean BMI for Group A was 24.98 ± 1.19 kg/m^{2,} and for Group B it was 25.40 ± 1.32 kg/m^2. Baseline GAG scores were comparable, with Group A scoring 23.48 ± 3.39 and Group B scoring 24.21 ± 3.25. Mean duration of acne in group A was 3.23±1.36 years, while 2.80±1.43 years in group B.

Gender distribution showed that Group A had 20 males (35.7%) and 36 females (64.3%), while Group B included 23 males (41.1%) and 33 females (58.9%). The rest of the demographic distribution can be viewed in Table 1. The location of acne vulgaris varied, with the forehead affected in 10 (17.9%) and 11 (19.6%) participants in Groups A and B, respectively. The right cheek was the most common site, affecting 24 (42.9%) in Group A and 25 (44.6%) in Group B.

Post-treatment GAG score was 10.43 ± 5.53 in Group A and 8.75 ± 5.99 in Group B, with no notable difference found between both groups (P = 0.12) (Table 2). Stratifications are presented from Table 3 to Table 11.

Table 1: Demographics

Demographics		Groups			
		Group A		Group B	
		n	%	n	%
Gender	Male	20	35.7%	23	41.1%
	Female	36	64.3%	33	58.9%
Education	Educated	34	60.7%	30	53.6%
	Uneducated	22	39.3%	26	46.4%
Occupation status	Employed	23	41.1%	27	48.2%
	Unemployed	33	58.9%	29	51.8%
Residence	Urban	37	66.1%	31	55.4%
	Rural	19	33.9%	25	44.6%
Socioeconomic status	Lower class	15	26.8%	14	25.0%
	Middle class	30	53.6%	32	57.1%
	Upper class	11	19.6%	10	17.9%
Location of acne vulgaris	Forehead	10	17.9%	11	19.6%
	Right cheek	24	42.9%	25	44.6%
	Left cheek	13	23.2%	15	26.8%
	Chest and upper back	9	16.1%	5	8.9%

Table 2: Comparison of post-treatment GAG score between both groups

	Groups	N	Mean	Std. Deviation	P value
GAG score post-treatment	Group A	56	10.43	5.533	0.12
	Group B	56	8.75	5.992	

Table 3: Stratification of comparison of GAG score between both groups with respect to age

Age groups (Years)		Groups	N	Mean	Std. Deviation	P value
18 to 35	GAG score post-treatment	Group A	43	11.05	5.686	0.003
		Group B	47	7.60	4.830	
36 to 50	GAG score post-treatment	Group A	11	7.82	4.557	0.01
		Group B	8	15.88	7.791	
51 to 60	GAG score post-treatment	Group A	2	11.50	4.950	0.53
		Group B	1	6.00	.	

Table 4: Stratification of comparison of GAG score between both groups with respect to gender

Gender		Groups	N	Mean	Std. Deviation	P value
Male	GAG score post-treatment	Group A	20	9.75	4.339	0.79

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		Group B	23	9.35	5.613	
Female	GAG score post-treatment	Group A	36	10.81	6.122	0.10
		Group B	33	8.33	6.293	

Table 5: Stratification of comparison of GAG score between both groups with respect to education

Education		Groups	N	Mean	Std. Deviation	P value
Educated	GAG score post-treatment	Group A (Continuous oral isotretinoin)	34	12.15	5.955	0.03
		Group B (Intermittent oral isotretinoin)	30	8.87	6.307	
Uneducated	GAG score post-treatment	Group A (Continuous oral isotretinoin)	22	7.77	3.504	0.55
		Group B (Intermittent oral isotretinoin)	26	8.62	5.728	

Table 6: Stratification of comparison of GAG score between both groups with respect to occupation status

Occupation status		Groups	N	Mean	Std. Deviation	P value
Employed	GAG score post-treatment	Group A (Continuous oral isotretinoin)	23	8.17	4.448	0.58
		Group B (Intermittent oral isotretinoin)	27	9.04	6.388	
Unemployed	GAG score post-treatment	Group A (Continuous oral isotretinoin)	33	12.00	5.728	0.01
		Group B (Intermittent oral isotretinoin)	29	8.48	5.699	

Table 7: Stratification of comparison of GAG score between both groups with respect to residence

Residence		Groups	N	Mean	Std. Deviation	P value
Urban	GAG score post-treatment	Group A (Continuous oral isotretinoin)	37	11.00	5.930	0.65
		Group B (Intermittent oral isotretinoin)	31	10.32	6.379	
Rural	GAG score post-treatment	Group A (Continuous oral isotretinoin)	19	9.32	4.607	0.09
		Group B (Intermittent oral isotretinoin)	25	6.80	4.924	

Table 8: Stratification of comparison of GAG score between both groups with respect to socioeconomic status

Socioeconomic status		Groups	N	Mean	Std. Deviation	P value
Lower class	GAG score post-treatment	Group A (Continuous oral isotretinoin)	15	10.33	5.563	0.63
		Group B (Intermittent oral isotretinoin)	14	9.21	6.874	
Middle class	GAG score post-treatment	Group A (Continuous oral isotretinoin)	30	10.60	5.703	0.01
		Group B (Intermittent oral isotretinoin)	32	7.38	4.499	
Upper class	GAG score post-treatment	Group A (Continuous oral isotretinoin)	11	10.09	5.522	0.41
		Group B (Intermittent oral isotretinoin)	10	12.50	7.663	

Table 9: Stratification of comparison of GAG score between both groups with respect to the location of acne vulgaris

Location of acne vulgaris		Groups	N	Mean	Std. Deviation	P value
Forehead	GAG score post-treatment	Group A (Continuous oral isotretinoin)	10	10.60	5.481	0.82
		Group B (Intermittent oral isotretinoin)	11	11.18	6.570	
Right cheek	GAG score post-treatment	Group A (Continuous oral isotretinoin)	24	10.83	6.005	0.16
		Group B (Intermittent oral isotretinoin)	25	8.36	6.170	
Left cheek	GAG score post-treatment	Group A (Continuous oral isotretinoin)	13	9.69	5.006	0.51
		Group B (Intermittent oral isotretinoin)	15	8.27	6.123	
Chest and upper back	GAG score post-treatment	Group A (Continuous oral isotretinoin)	9	10.22	5.826	0.23
		Group B (Intermittent oral isotretinoin)	5	6.80	1.789	

Table 10: Stratification of comparison of GAG score between both groups with respect to BMI

BMI (Kg/m2)		Groups	N	Mean	Std. Deviation	P value
18 to 24.9	GAG score post-treatment	Group A (Continuous oral isotretinoin)	30	11.73	5.889	0.01
		Group B (Intermittent oral isotretinoin)	23	7.52	6.632	
> 24.9	GAG score post-treatment	Group A (Continuous oral isotretinoin)	26	8.92	4.766	0.61
		Group B (Intermittent oral isotretinoin)	33	9.61	5.443	

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Table 11: Stratification of comparison of GAG score between both groups with respect to duration of acne

Duration of acne (Years)		Groups	N	Mean	Std. Deviation	P value
1 to 3	GAG score post-treatment	Group A (Continuous oral isotretinoin)	29	10.86	5.436	0.004
		Group B (Intermittent oral isotretinoin)	37	7.22	4.410	
> 3	GAG score post-treatment	Group A (Continuous oral isotretinoin)	27	9.96	5.701	0.36
		Group B (Intermittent oral isotretinoin)	19	11.74	7.519	

DISCUSSION

The efficacy and safety of low-dose continuous versus low-dose intermittent oral isotretinoin therapy in moderate acne vulgaris have been explored in multiple studies, each offering unique insights into treatment outcomes. Our study compared continuous isotretinoin and intermittent isotretinoin, revealing comparable baseline demographics but distinct post-treatment outcomes.

The mean age in Group A was 30.71 ± 10.13 years, while Group B averaged 29.43 ± 8.55 years, with no notable differences in BMI or baseline GAG scores. Post-treatment, Group A showed a GAG score of 10.43 ± 5.53, whereas Group B showed 8.75 ± 5.99, with no notable difference. This suggests both regimens are effective, though in contrast, Shetti et al. reported significant improvements in GAG scores with continuous therapy (13).

Demographic variables such as gender, education, and residence were balanced across groups in our study. Our female majority in both groups (64.3% in Group A, 58.9% in Group B) parallels Niazi et al's cohort, where the majority of their patients in both groups were females. Maheshwari et al. documented a higher number of female patients with acne in their study, highlighting acne's prevalence among females (15). Similarly, Dhubaibi et al in their study also documented a higher prevalence of female acne patients (16). Faghihi et al. also reported that the frequency of female patients was higher in their trial, which compared low and conventional doses of oral isotretinoin for acne (17).

However our employment and socioeconomic distributions differed with higher unemployment in Group A (58.9%) versus Group B (51.8%), we also noted that majority of the participants belonged to the middle class in both groups. Around 26.8% in group A and 25% in group B belonged to the lower class of economic background, a factor not extensively addressed in other studies but can potentially influence treatment adherence and outcomes.

The location of acne lesions in our study, predominantly on the cheeks (42.9% in Group A and 44.6% in Group B), aligns with Maheshwari et al, as they reported that cheeks were the most affected area of acne across their cohort (15). In Dhubaibi et al's study, facial acne was the primary focus (16). Notably, our chest and upper back involvement (16.1% in Group A and 8.9% in Group B) was less severe, which could be due to our inclusion criteria, where we only enrolled patients with moderate acne.

Post-treatment GAG scores in our study demonstrated a non-significant trend favoring both therapies, contrasting with Faysal et al, who found intermittent therapy superior in their trial ($p = 0.006$) (18). Although both studies, ours and Faysal et al's, employed the same dosing regimen for intermittent therapy. Similarly, Niazi et al reported comparable efficacy between daily and alternate-day low-dose isotretinoin, reinforcing that lower doses can achieve similar results with fewer side effects (14). A recent study also highlighted identical findings, as they reported that both daily and intermittent low doses are equally effective for the treatment of acne (19).

Leena et al. documented better efficacy with high doses of isotretinoin, but they reported that it has more side effects when compared to lower doses. They noted higher dryness of eyes with conventional doses than with low doses (20). Faghihi et al. also highlighted that dose-dependent side effects in conventional-dose patients were higher than in low-dose groups, underscoring the safety of reduced dosing (17).

Comparative analysis reveals that while intermittent therapy reduces side effects, continuous low-dose regimens may offer more consistent efficacy, particularly in moderate acne (13, 16). We recommend a middle ground, which is continuous therapy for moderate acne with scarring risk and intermittent treatment for milder cases or maintenance.

We suggest that both continuous and intermittent low-dose isotretinoin are viable for mild to moderate acne, with continuous therapy potentially offering slight clinical advantages. However, sporadic regimens remain valuable for reducing side effects and improving compliance. Clinicians should weigh these factors against individual patient needs, considering severity, psychosocial impact, and risk of scarring. Larger long-term studies are needed to refine protocols and optimize outcomes across diverse populations.

CONCLUSION

In conclusion, low-dose continuous and low-dose intermittent oral isotretinoin therapy are equally effective in the treatment of moderate acne vulgaris.

DECLARATIONS

Data Availability Statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned. (IRB)

Consent for publication

Approved

Funding

Not applicable

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

NEEZAH NOOR (Postgraduate Resident)

Conceived the study, contributed to data collection, analysis, and drafted the manuscript

SUMMAYA SALEEM (Assistant Professor)

Provided supervision, critical review of study design, and revised the manuscript for important intellectual content, and final approval of the draft.

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Critical input and review of literature
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Review of literature
All authors read and approved the final version of the manuscript.

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