ORIGINAL ARTICLE

OPEN LABEL STUDY COMPARING THE EFFICACY OF CONTINUOUS LOW DOSE ISOTRETINOIN VERSUS INTERMITTENT LOW DOSE ISOTRETINOIN REGIMENS IN MODERATE TO SEVERE ACNE VULGARIS

Farhat Rehman[1], Durreshehwar Arshad Pirzada[2]✉, Sumaira Abdullah[1], Mahvish Aftab Khan[3]

[1]Akbar Niazi Teaching Hospital Islamabad-Pakistan
[2]Ayub Teaching Hospital Abbottabad-Pakistan
[3]Pakistan Institute of Medical Sciences, Islamabad-Pakistan

Background: Acne vulgaris, recognized as the eighth most prevalent disease globally, affects approximately 9.4% of the world population. It can manifest in a spectrum ranging from mild physiologic acne to severe presentations such as nodules, cysts, and abscesses. This open-label comparative study was conducted at the Dermatology OPD of Akbar Niazi Teaching Hospital, Islamabad, from September 1, 2021, to March 1, 2022, with the objective of evaluating the efficacy of low-dose continuous versus low-dose intermittent oral isotretinoin in patients with moderate-to-severe acne vulgaris. Acne was defined by the presence of lesions including papules, pustules, comedones or cysts with a Global Acne Grading System (GAGS) score of 19–30 indicating moderate and 31–38 indicating severe cases. Efficacy was defined as a greater than 80% reduction in the GAGS score after three months of treatment, calculated as: percentage decrease = total decrease in score / baseline score ×100. The hypothesis stated that a difference exists in efficacy between the two isotretinoin regimens. **Methods:** A total of 60 patients of both gender with Acne vulgaris were included in the study. Patients were divided in two groups. Each group had 30 patients. The initial assessment of acne was done by using GAGS score. In group A, patients were prescribed 20 mg oral isotretinoin once daily for 6 months and in Group B patients were prescribed intermittent regimen - 20 mg oral isotretinoin on alternate day for 6 months. Efficacy was noted by lesion counts from both groups, on monthly basis for 3 months and a follow up visit at 6 months. **Results:** Age range in this study was 18 to 40 years with mean age of 24.866±3.29 years and mean GAGS score was 28.266±2.79 in Group A and mean age of 25.266±3.67 years and mean GAGS score was 28.533±3.12 in Group B. Efficacy was observed in 27 (90%) patients in group A as compared to 25 (83.3%) patients in group B (p=0.447). **Conclusion:** In conclusion, the present study demonstrates that the low-dose continuous and low-dose intermittent oral isotretinoin regimens have comparable efficacy at the end of treatment.

Keywords: Acne vulgaris; isotretinoin; Efficacy

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INTRODUCTION

Acne vulgaris is one of the top ten most prevalent diseases globally. Previous studies have found the prevalence of acne vulgaris to be 9.4% worldwide and in Pakistan the prevalence rate of acne is found to be 5%.[1,2] It is the inflammatory disorder of pilosebaceous unit. Lesions of acne range from mild non-inflammatory lesions like papules to severe inflammatory lesions like pustules and Nodulocystic lesions. Complications like scarring can lead to social embarrassment and psychological stress[3], therefore significantly affecting the quality of life[4]. Pathophysiology of acne is determined by various genetic, hormonal, inflammatory and dietary factors. Dietary factors include refined carbohydrates, dairy products and nuts.[5,6] Various lifestyle factors like mental stress, reduced sleep, cigarette smoking, lack of exercise and obesity[6] are important factors contributing to pathophysiology of acne. Among the various complications of acne scarring is the most debilitating complication which impairs mental health and has significant effect on quality of life of the individuals. And it is of note that complications like scarring have strong association with family history.[7] The treatment options for acne include topical and systemic retinoids, antibiotics and topical anti-inflammatory and bactericidal agents like benzoyl peroxide.[8] Retinoids are vitamin A derivatives which are used as first line treatment for acne vulgaris.

Retinoids decrease the sebum production, prevent and control growth of the comedones, improve the epidermal turnover and also treat and prevent post acne hyperpigmentation and scarring.[8] The standard dose of isotretinoin is 0.5–1.0 mg/kg/day which when given for 16–32 weeks cause many systemic and mucocutaneous side effects including dryness of mucosae, cheilitis, myalgias, increase in serum triglycerides and rarely pseudotumor cerebri.[9] Various studies have suggested that these adverse effects can be avoided by administering the isotretinoin on alternate days. The alternate day dosing had comparable efficacy to daily oral isotretinoin dosing as proven by study conducted by Dhaked DR *et al* which showed that efficacy of fixed dose of 20 mg/day of isotretinoin was 98.3% compared to 93.96% with alternate day dose of 20 mg/day.[10] There are few randomized comparative studies of low dose regimens of oral isotretinoin in the Pakistani literature. Results of our study will help to select better dosage regimen of oral isotretinoin therapy in moderate-to-severe acne vulgaris in our general population.

MATERIAL AND METHODS

This open label comparative study was conducted from 1st September 2021 to 1st March 2022 at Department of Dermatology, Akbar Niazi Teaching Hospital, Islamabad. Sample size was calculated with WHO sample size calculator using alpha= 5% (two-sided) with power = 90%. By using expected proportion(efficacy) in population 1=50%[10] and expected proportion in population 2=93.96%[20].Total sample size was 60,which was divided into two groups.30 sample size for low dose continuous group or group A and 30 sample size for low dose intermittent group or group B

The patients meeting the following inclusion criteria were included in the study: Patients aged 18 to 40 years of either gender presenting to dermatology outpatient department having moderate to severe acne and were treatment naïve, with no co morbidities and were included in the study after taking permission from ethical committee. Patients having underlying dyslipidaemia (fasting triglyceride levels >150 mg/dl), underlying liver disease, pregnancy, married women with chances of getting pregnant and who had used isotretinoin in past were excluded from the study. A total 60 patients who met the inclusion criteria were included in the study and were divided into two groups, i.e., group A and B. Both groups had 30 patients each by simple random sampling technique. Patients in group A were given low dose isotretinoin 20 mg daily while patients in group B were given low dose isotretinoin 20 mg on alternate days. The patients were followed up every 4th week during the treatment period. Efficacy was defined as >80% decrease in global acne grading score (GAGS) 6 months after starting the intervention from both groups and recorded on specially designed *proforma.*

RESULTS

Age range in this study was 18 to 40 years with mean age of 24.866±3.29 years, mean duration of disease 4.600±2.52 months and mean GAGS score was 28.266±2.79 in Group A and mean age of 25.266±3.67 years, mean duration of disease 3.266±1.77 months and mean GAGS score was 28.533±3.12 in Group B as shown in Table-1.

Female gender was dominant in both groups as shown in Table-2.

Efficacy was observed in 27 (90%) patients in group A as compared to 25 (83.3%) patients in group B (p= 0.447) as shown in Table-3.

Stratification of efficacy in both groups with regards to age, gender, duration of disease and GAGS score shown in Table-4.

Table-1: Mean±SD of patients according to age, duration of disease and GAGS score
n=60

Demographics	Group A n=30 Mean ±SD	Group B n=30 Mean ±SD
Age (years)	24.866±3.29	25.266±3.67
Duration of disease (months)	4.600±2.52	3.266±1.77
GAGS score	28.266±2.79	28.533±3.12

Table-2: Frequency and percentage of gender in both groups

Gender		n=30 Group A	n=30 Group B
1	Male	4 (13.3%)	6 (20%)
2	Female	26 (86.7%)	24 (80%)
	Total	30 (100%)	30 (100%)

Table-3: Comparison of efficacy in both groups

Efficacy		n=30 Group A	n=30 Group B	P Value
1	Yes	27 (90%)	25 (83.3%)	0.447
2	No	3 (10%)	5 (16.7%)	
	Total	30 (100%)	30 (100%)	

Table-4: Stratification of efficacy with respect to GAGS score in both groups
For Moderate

Group	Efficacy		P value
	Yes	No	
A	20 (87%)	3 (13%)	**0.853**
B	17 (85%)	3 (15%)	

For Severe

Group	Efficacy		P value
	Yes	No	
A	7 (100%)	0 (0%)	**0.207**
B	8 (80%)	2 (20%)	

DISCUSSION

Acne vulgaris is the most common skin disease affecting mostly the adolescents and young adults. Topical and systemic retinoids are the main stay of treatment in addition to antibiotics which should always be prescribed in combination with benzoyl peroxide for no more than 12 weeks [11] Results of our study showed that isotretinoin when given in daily or alternate day regimen gives comparable clinical results after 3 months of treatment as endorsed by Layton *et al* [12]. Their study also showed that when patients were given isotretinoin for treating acne clinical improvement was achieved after 4 months of treatment. The study further showed that 10 years post treatment 61% of the patients were virtually disease free and 23% of the patients required a second course of isotretinoin and that relapse was seen more in patients with truncal acne however age, gender, and duration of acne had no effect on relapse of acne.[12]

It is highlighted in various studies that despite several adverse effects including teratogenicity, isotretinoin induces complete/near complete remission in patients with both scarring and non-scarring acne vulgaris.[13] The above mentioned results were endorsed by various studies which showed that isotretinoin can cause various adverse effects like dry chapped lips ,epistaxis, xerosis, dyslipidaemia, raised liver enzymes and DISH (diffuse idiopathic skeletal hyperostosis) however these adverse effects are dose dependent and may be reduced by using the lower doses of systemic isotretinoin.[13,14] In our study only two participants from group A reported significant side effects i.e. elevated triglycerides, AST and ALT as compared to group B in which no side effect was reported. The patient satisfaction score was highest in group B then group A possibly due to fewer side effects with low-dose intermittent treatments and more tolerability.

Because of abovementioned side effects and the necessity of long-term daily use, patients often have difficulty complying with the standard daily dose of isotretinoin 0.5–1.2 mg/kg daily for 16–32 weeks with cumulative dose of 120 mg/kg. In an effort to overcome these limitations, low dose daily or intermittent dose regimens have been introduced in recent studies. In his study the drug remained effective, complete improvement was seen in 82.9% of the patients receiving low dose intermittent isotretinoin with mild adverse effects which did not warrant any discontinuation of the treatment. similar results were observed in our study.

The results of this study conducted by Y Kaymak *et al*[15] are also supported by results from our study in which 20 mg isotretinoin when given on alternate day showed 83.3%efficacy.

Various studies have also supported the efficacy and safety of intermittent low dose isotretinoin regimen in treatment of Acne vulgaris.[16–19] To our knowledge there have been no previous studies comparing all isotretinoin therapeutic regimens simultaneously.

The aim of our study was to compare the efficacy of low dose continuous and low-dose intermittent oral isotretinoin therapy in moderate-to-severe acne vulgaris. By carrying out a 3-month follow-up evaluation, we also investigated the recurrence rate and efficacy of each regimen. In our study, all regimens showed efficacy based on investigator's evaluation using GAGS scores. We verified that the low dose continuous and low-dose intermittent oral isotretinoin had similar effects in the GAGS scores. Intermittent treatment was found to have little less efficacious, but the difference was not statistically significant. For inflammatory and noninflammatory lesions, the low-dose intermittent regimen had similar effects as compared to the low dose continuous regimen. These results suggest that the low dose continuous and low-dose intermittent oral isotretinoin regimens have similar efficacy as both show similar reductions in the number of inflammatory and noninflammatory lesions during the treatment period. Adverse effects may be more frequent with low dose continuous regimen as compared with low-dose intermittent regimen.

In our study none of the patient from group B showed any adverse effect which suggests that the low-dose regimens are superior to other regimens in terms of side effect profile and safety. On the contrary patients on high dose regimens have less relapse of the disease. The intermittent regimen needs a long treatment period to reach a high cumulative dose; therefore, relapse is common with this regimen. Our study doesn't have a long term follow up period and doesn't provide enough data regarding long term remission induced by intermittent isotretinoin therapy. Further studies are needed to evaluate the efficacy, safety and induction of long-term remission by low dose intermittent isotretinoin treatment.

CONCLUSION

The present study demonstrates that the low-dose continuous and low-dose intermittent oral isotretinoin regimens have similar efficacy after the end of treatment. Although intermittent treatment is convenient and tolerable for patients, they have relatively high risk of relapse in this group. These results suggest that, when we consider tolerability, efficacy and patient satisfaction, the low-dose treatment regimen is the most suitable for patients with moderate to severe acne.

AUTHORS' CONTRIBUTION

FR: Conceptualization of study design, data collection, literature search. DAP: Conceptualization of study design, literature search, data analysis, data interpretation, write-up, proof reading. SA: Conceptualization of study design, data collection, proof reading. MA: Literature search, data analysis

REFERENCES

1. Babar O, Mobeen A. Prevalence and psychological impact of acne vulgaris in female undergraduate medical students of Rawalpindi and Islamabad, Pakistan. Cureus 2019;11(9):e5722.
2. Hay RJ, Johns NE, Williams HC. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. J Invest Dermatol 2014;134(6):1527–34.
3. Abo El-Fetoh NM, Alenezi NG, Alshamari NG, Alenezi OG. Epidemiology of acne vulgaris in adolescent male students in Arar, Kingdom of Saudi Arabia. J Egyptian Public Health Assoc 2016;91(3):144–9.
4. Alanazi MS, Hammad SM, Mohamed AE. Prevalence and psychological impact of Acne vulgaris among female secondary school students in Arar city, Saudi Arabia, in 2018. Electron Physician 2018;10(8):7224–9.
5. Baldwin H, Tan J. Effects of Diet on Acne and Its Response to Treatment. Am J Clin Dermatol 2021;22(1):55–65.
6. Alshammrie FF, Alshammari R, Alharbi RM, Khan FH, Alshammari SK. Epidemiology of acne vulgaris and its association with lifestyle among adolescents and young adults in Hail, Kingdom of Saudi Arabia: a community-based study. Cureus 2020;12(7):e9277.
7. Liu L, Xue Y, Chen Y, Chen T, Zhong J, Shao X, *et al*. Prevalence and risk factors of acne scars in patients with acne vulgaris. Skin Res Technol 2023;29(6):e13386.
8. Vasam M, Korutla S, Bohara RA. Acne vulgaris: A review of the pathophysiology, treatment, and recent nanotechnology-based advances. Biochem Biophys Rep 2023;36:101578.
9. Leyden JJ, Del Rosso JQ, Baum EW. The use of isotretinoin in the treatment of acne vulgaris: clinical considerations and future directions. J Clin Aesthet Dermatol 2014;7(2 Suppl):S3–21.
10. Dhaked DR, Meena RS, Maheshwari A, Agarwal US, Purohit S. A randomized comparative trial of two low-dose oral isotretinoin regimens in moderate to severe acne vulgaris. Indian Dermatol Online J 2016;7(5):378–85.
11. Oge' LK, Broussard A, Marshall MD. Acne Vulgaris: Diagnosis and Treatment. Am Fam Physician 2019;100(8):475–84.
12. Layton AM, Knaggs H, Taylor J, Cunliffe WJ. Isotretinoin for acne vulgaris--10 years later: a safe and successful treatment. Br J Dermatol 1993;129(3):292–6.
13. Tahir CM. Efficacy and adverse effects of systemic isotretinoin therapy. J Pak Assoc Dermatol 2011;21(1):38–42.
14. Graf SW, Whittle SL. Isotretinoin-induced skeletal hyperostosis. Springerplus 2014;3:698.
15. Kaymak Y, Ilter N. The effectiveness of intermittent isotretinoin treatment in mild or moderate acne. J Eur Acad Dermatol Venereol 2006;20(10):1256–60.
16. Amichai B, Shemer A, Grunwald MH. Low-dose isotretinoin in the treatment of acne vulgaris. J Am Acad Dermatol 2006;54(4):644–6.
17. Mandekou-Lefaki I, Delli F, Teknetzis A, Euthimiadou R, Karakatsanis G. Low-dose schema of isotretinoin in acne vulgaris. Int J Clin Pharmacol Res 2003;23(2-3):41–6.
18. Akman A, Durusoy C, Senturk M, Kic CK, Soyturk D, Alpsoy E. Treatment of acne with intermittent and conventional isotretinoin: a randomized, controlled multicenter study. Arch Dermatol Res 2007;299(10):467–73.
19. Cunliffe WJ, van de Kerkhof PC, Caputo R, Cavicchini S, Cooper A, Fyrand OL, *et al*. Roaccutane treatment guidelines: results of an international survey. Dermatology 1997;194(4):351–7.
20. Agarwal US, Besarwal RK, Bhola K. Oral isotretinoin in different dose regimens for acne vulgaris: a randomized comparative trial. Indian J Dermatol Venereol Leprol. 2011 Nov-Dec;77(6):688-94. doi: 10.4103/0378-6323.86482. PMID: 22016276.

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Address for Correspondence:

Durreshehwar Arshad Pirzada, Department of Dermatology, Ayub Teaching Hospital, Abbottabad-Pakistan
Cell: +92 321 526 6452
Email: drshehwar@hotmail.com