

Efficacy of oral isotretinoin in combination with desloratadine versus oral isotretinoin alone in the treatment of moderate acne vulgaris

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Abstract

Objective To compare the efficacy of oral isotretinoin used alone versus used in combination with desloratadine for moderate acne vulgaris.

Methods It is a randomized controlled trial conducted at the Department of Dermatology Unit-I, Mayo Hospital, Lahore from October 25, 2020 to April 25, 2021. A total 108 patients between the ages of 15-35 years who had moderate acne vulgaris (as defined by Global Acne Grading System score of 19-30) were enrolled. Group-A was prescribed Oral Isotretinoin 20mg along with desloratadine 5mg, while Group-B was given oral Isotretinoin 20 mg only. At baseline, pre-treatment Global Acne Grading System (GAGS) score was calculated. Patients of both groups were examined at 4, 8, and 12 weeks and final evaluation was done at 16 weeks of treatment. Efficacy was defined as >90% reduction in GAGS score. Percentage reduction in the GAGS score was calculated and efficacy scaled at the final visit at 16th week of treatment.

Results In group-A, 13(24.1%) were males and 41(75.9%) were females and in group-B, 16(29.6%) were males and 38(70.4%) were females. The average age of patients in group-A was 21.7±3.2 years while in group-B was 22.5±3.3 years. In group-A, 42(77.8%) had efficacy while in group-B, 28(51.9%) had efficacy with a p-value 0.005, which is statistically significant.

Conclusion For treating moderate acne vulgaris, combining oral Isotretinoin with desloratadine augments the curative effect of isotretinoin as compared to using isotretinoin only.

Key words

Acne vulgaris; Isotretinoin; Desloratadine.

Introduction

Acne vulgaris is a common inflammatory condition of pilosebaceous units, affecting up to 85% of the adults at some point of their lives.¹⁻³

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It is more prevalent among adolescents and young adults, but it is now being increasingly identified in adult population as well.⁴ Majority of the lesions occur on face, and can lead to profound psychosocial stress such as feeling of anxiety, low self-worth, and depression among the affected population, apart from being a financial burden.⁵⁻⁹

The pathogenesis of acne vulgaris classically involves increased sebaceous gland activity with

seborrhea, hyperkeratotic infundibulum of the follicle, proliferation of *Propionibacterium acnes* along with increased perifollicular inflammatory response.¹⁰⁻¹³ Currently isotretinoin, a retinoid which targets all these etiological factors of acne vulgaris, is recommended systemically for the management of moderate to severe and nodulocystic acne, acne conglobata, acne fulminans and other recalcitrant cases.¹⁴⁻¹⁶

However, its use is associated with several adverse effects, such as xerosis of the skin, cheilitis, dry eyes, epistaxis, erythematous skin rashes, alopecia, birth defects, deranged liver function tests, dyslipidemias, nausea, papilledema, lethargy and hematological abnormalities.¹⁵⁻¹⁷ Antihistamines, specifically H1-blockers, have long been used for pruritic dermatosis. Recently, they have been experimentally used as an adjunct with isotretinoin for the treatment of acne vulgaris.^{1-3,18,19}

In the study by Van TN *et al.* on Vietnamese patients, the patients of moderate Acne vulgaris who were given a combination of oral isotretinoin and desloratadine (an H1 blocker) had an enhanced complete curative rate (45.2%) versus the control group which was given oral isotretinoin only (22.6%).¹

Similarly in the study conducted by D Pandey on Nepalese patients, oral isotretinoin combined with levocetirizine led to a statistically significant reduction in GAGS score (51.0 vs. 38.5%) as compared to isotretinoin only group.³

P. acnes alters and affects the pH of the microenvironment of pilosebaceous unit which leads to production of histamine, by mast cells, basophils and keratinocytes.²⁰⁻²⁷ Histamine receptors have been identified in the sebocytes by Pelle E *et al.*;²⁴ on which anti-histamines act to decrease the production of squalene, the

precursor of sebum production. Anti-histamines also inhibit inflammatory mediators (IL-4, IL-6 etc.)^{25,31} and counter the muco-cutaneous side-effects of isotretinoin like rashes and itching, making it more acceptable to the patient.^{1,3}

This study was done to demonstrate the effectiveness of anti-histamine desloratadine as an adjuvant to isotretinoin for treating moderate acne vulgaris in Pakistani population presenting to Mayo Hospital, Lahore. No local literature is currently available on this topic. The combination therapy proved to be slightly more cost-effective due to decrease in the duration of treatment by enhancing the curative efficacy of isotretinoin.

Methods

After obtaining approval from ethical committee, 108 cases between the ages of 15-35, of moderate acne as defined by a baseline GAGS score of 19-30, who had not taken any prior treatment for acne and had no contraindication to the use of either isotretinoin or desloratadine, were enrolled from the Outpatient Department of Dermatology Unit-I, Mayo Hospital Lahore. After obtaining a written consent, bio-data was recorded on a pre-designed proforma. Patients were allocated randomly by lottery method into Group-A (studied group) and B (control group).

Group-A was prescribed Oral Isotretinoin 20mg along with desloratadine 5mg, while Group-B was given oral Isotretinoin 20 mg only. At baseline, pre-treatment GAGS score was calculated and photographs were taken by Samsung Galaxy J7 camera from a distance of 6-8 inches from the face. Patients of both groups were evaluated at 4, 8 and 12 weeks of treatment and final evaluation was done at 16 weeks of treatment.

GAGS scoring was done at each visit by the

same dermatologist. Photographs were taken again at the end of 16th week of treatment. Percentage reduction in the GAGS score was calculated and efficacy scaled at the final visit at 16th week of treatment. Patients were not allowed to use any other topical or systemic treatment for acne vulgaris throughout the treatment.

The data were entered and analysed with SPSS v25.0. Quantitative variables like age, BMI and GAGS score were presented as mean and SD. Qualitative variables such as gender and treatment efficacy were presented as frequencies and percentages. For comparison of two groups, chi-square test was applied. A p-value ≤ 0.05 was taken as significant. Data were stratified for gender, age, BMI and GAGS score at baseline to deal with effect modifiers. Post-stratification, chi-square test was applied taking p-value ≤ 0.05 as significant.

Results

In group-A (Oral Isotretinoin plus

desloratadine), 13 (24.1%) were males and 41 (75.9%) were females and in group-B (Oral Isotretinoin alone), 16 (29.6%) were males and 38 (70.4%) were females.

In group-A, the average age of patients was 21.7 \pm 3.2 years while in group-B was 22.5 \pm 3.3 year. In group-A, 38 (70.4%) patients had ages between 18-25 years and 16 (29.6%) between 26-35 years, while in group-B, 34 (63.0%) patients had ages between 15-25 years and 20 (37.0%) between 26-35 years.

In group-A, 4 (7.4%) were underweight, while 45(83.3%) were normal and 5(9.3%) were overweight. In group-B, 6 (11.1%) patients were underweight, while 41 (75.9%) were normal and 7 (13.0%) were overweight (**Table 1**).

In group A, the mean GAGS score at baseline was 23.48 \pm 3.07 whereas in group-B, it was 23.76 \pm 3.44. At the end of 16th week, the mean GAGS score of group A was 1.35 \pm 1.63 and of group B was 4.00 \pm 3.40 (**Table 2**).

Table 1 Baseline characteristics of the groups.

	Group-A (Oral Isotretinoin plus Desloratadine)	Group-B (Oral Isotretinoin alone)	Total (n=108)
Gender			
Male	13 (24.1%)	16 (29.6%)	29 (26.9%)
Female	41 (75.9%)	38 (70.4%)	79 (73.1%)
Total	54 (100%)	54 (100%)	108 (100%)
Age groups			
15-25 years	38 (70.4%)	34 (63.0%)	72 (66.7%)
26-35 years	16 (29.6%)	20 (37.0%)	36 (33.3%)
Total	54 (100%)	54 (100%)	108 (100%)
Body mass index (BMI)			
Underweight (BMI<18.5)	4 (7.4%)	6 (11.1%)	10 (9.3%)
Normal (BMI 18.5-24.9)	45 (83.3%)	41 (75.9%)	86 (79.6%)
Overweight (BMI>25)	5 (9.3%)	7 (13.0%)	12 (11.1%)
Total	54 (100%)	54 (100%)	108 (100%)

Table 2 Mean GAGS score at baseline and at week 16.

GAGS Score	Group A	Group B
Week 0	23.48 \pm 3.07	23.76 \pm 3.44
Week 16	1.35 \pm 1.63	4.00 \pm 3.40

In group-A, 20 (37%) had excellent outcome, 22 (40.8%) had good, 11 (20.4%) had fair and 1 (1.8%) had moderate outcome. In group-B, 10 (18.5%) had excellent outcome, 18 (33.3%) had

Table 3 Comparison of outcome distribution between the groups.

Outcome	Group-A (Oral Isotretinoin plus Desloratadine)	Group-B (Oral Isotretinoin alone)	Total (n=108)
Excellent (100% reduction in GAGS score)	20 (37%)	10 (18.5%)	30 (27.8%)
Good (>90% reduction in GAGS score)	22 (40.8%)	18 (33.3%)	40 (37.0%)
Fair (75-90% reduction in GAGS score)	11 (20.4%)	20 (37%)	31 (28.7%)
Moderate (50-75% reduction in GAGS score)	1 (1.8%)	6 (11.1%)	7 (6.5%)
Total	54 (100.0%)	54 (100.0%)	108 (100.0%)

Table 4 Comparison of efficacy between groups.

Efficacy	Group-A (Oral Isotretinoin plus Desloratadine)	Group-B (Oral Isotretinoin alone)	Total (n=108)	p-value
Yes	42 (77.8%)	28 (51.9%)	70 (64.8%)	0.005
No	12 (22.2%)	26 (48.1%)	38 (35.2%)	
Total	54 (100%)	54 (100%)	108 (100%)	

good, 20 (37%) had fair and 6 (11.1%) had moderate outcome (**Table 3**).

In group-A, 42 (77.7%) had efficacy while in group-B, 28 (51.9%) had efficacy with a p-value 0.005, which is statistically significant (**Table 4**).

Discussion

From the demographic results, acne vulgaris is one of the commonest skin conditions, affecting about 9.4% of the total world population.³³ The maximum incidence occurs between the ages of adolescence and post adolescence (18-35 years).^{4,33} Acne vulgaris is a common skin disease of adolescence; it affects about 90% of adolescents primarily, then its incidence decreases, but acne may persist up to the age 35 years or older.^{4,28,33} It has a marked psychosocial morbidity, apart from the financial costs incurred in treatment.⁵⁻⁹

Studies show that in acne, perifollicular inflammation starts before the development of clinically apparent lesions, and persists at all stages.^{12,29,30} The inflammatory response is marked by the upsurge of mediators, of which leukotrienes and most importantly, histamine are the main mediators.^{12,25,31}

Therefore, antihistamines can reduce inflammation by inhibiting histamine, thereby reducing new lesion formation and assisting in resolving the already developed acne.¹⁻³

Study by Schroeder JT *et al.* has shown that desloratadine acts as an inhibitor of several mediators of inflammation which include histamine, interleukins (IL-4, IL-6, IL-8, IL-13), leukotrienes, prostaglandins and tryptase.³¹

Thus, desloratadine, a second-generation antihistamine, acts like an anti-inflammatory agent. Also, Pelle *et al.* demonstrated that desloratadine reduces squalene formation, which is an important component of the sebum.^{24,32}

In the study done by Van TN *et al.* on Vietnamese patients of moderate acne vulgaris as defined by a GAGS score of 19-30, in the group using Isotretinoin 20mg with desloratadine 5mg, there was significant lowering of the average number of inflammatory lesions (0.19 vs. 0.94) than that in the group using only isotretinoin, with a p value <0.025.¹ However, there was no significant reduction in non-inflammatory lesions. By the end of the study at week 16, the mean GAGS score of the Isotretinoin with desloratadine group was lower than that of Isotretinoin only group (3.62±2.33

vs. 7.21 ± 3.59), with $p = 0.001$. The patients of moderate acne vulgaris who were given a combination of oral isotretinoin and desloratadine had a greater rate of complete cure (45.2%) versus the group which was given oral isotretinoin only (22.6%).¹

In our study, in group A (Oral Isotretinoin plus desloratadine), the mean GAGS score at week 0 was 23.48 ± 3.07 whereas in group-B (Oral Isotretinoin alone), it was 23.76 ± 3.44 . At the end of 16th week, the average GAGS score of group A was 1.35 ± 1.63 and of group B was 4.00 ± 3.40 .

At the end of 16 weeks, both groups had good results: patients of group A achieved 37% excellent, 40.8% good and 20.4% fair response; the results in patients of group B were 18.5%, 33.3%, and 37%, respectively. Hence, our conclusion was desloratadine group fared better ($p=0.005$).

Similarly, in Lee's study, a randomized controlled comparative study conducted on 40 patients, at week 12, the patients given isotretinoin and desloratadine showed a greater decrease in acne lesion count (45.6%) as compared with patients given isotretinoin only (18.7%) ($p < 0.05$) which reached statistical significance.² Similarly, a substantial reduction in GAGS score which was significant statistically, was seen in the desloratadine with isotretinoin group as compared to the isotretinoin only group. The combination arm had 40% of patients clearing acne, with 50% showing improvement whereas the control group had 20% of the cases clearing acne, and 40% showing improvement. The greater decrease of GAGS scores in the studied arm was evident from week 2 but reached statistically significant change from week 4.²

In the study by D Pandey conducted on

Nepalese patients, combination of isotretinoin and levocetirizine resulted in a statistically significant decrease in GAGS score (51.0 vs. 38.5%) as compared to isotretinoin only group. There was also a significant decrease in acne lesion count; 63.2% reduction in comedones in study group as compared to 44.5% in isotretinoin only group; for inflammatory acne lesions: 75.9 reduction as compared to 62.7% in control group; for total number of lesions: 66.07 (study group) vs. 48.7% (control group).³

Yosef's study showed similar results.¹⁸ In this study by Yosef *et al*; isotretinoin was used with antihistamine levocetirizine hydrochloride (5mg/day). 72% of isotretinoin and anti-histamine treated patients showed complete cure at the end of 16 weeks, whereas only 28% of isotretinoin-only group showed similar cure ($p=0.005$), similar to our study.

Dhaheer SA and Jasim's study showed almost similar result of 50% excellent, 39.5% good in the combination group whereas the control group showed 31.6% excellent, and 34.2% good.¹⁹

Similar to the results concluded in these studies, in our study, in group-A, 42(77.8%) had efficacy (>90% reduction in GAGS score), while in group-B, 28(51.9%) had efficacy with a p-value 0.005, which is statistically significant.

Conclusion

For treating moderate acne vulgaris, combining oral Isotretinoin with desloratadine augments the curative effect of isotretinoin as compared to using isotretinoin only.

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent.

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Conflict of interest Authors declared no conflict of interest.

Author's contribution

MM, AL: Substantial contributions to concept, study design, acquisition of data and analysis and interpretation of data, manuscript writing and final approval for the version to be published.

WS, FA: Substantial contribution to concept and study design, critical review and final approval for the version to be published.

FNK, QuA: Substantial contribution to acquisition of data, manuscript writing and final approval for the version to be published.

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