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ORIGINAL RESEARCH ARTICLE

Efficacy and Safety of Tazarotene 0.1% Plus Clindamycin 1% Gel Versus Adapalene 0.1% Plus Clindamycin 1% Gel in Facial Acne Vulgaris: A Randomized, Controlled Clinical Trial

Rituparna Maiti[1] · Chandra Sekhar Sirka[2] · M. A. Ashique Rahman[3] ·
Anand Srinivasan[1] · Sansita Parida[4] · Debasish Hota[1]

Abstract

Background Acne vulgaris is a multifactorial disorder which is ideally treated with combination therapy with topical retinoids and antibiotics.

Objectives The present study was conducted to compare the efficacy and safety of tazarotene plus clindamycin against adapalene plus clindamycin in facial acne vulgaris.

Methods This study is a randomized, open-label, parallel design clinical trial conducted on 60 patients with facial acne at the outpatient dermatology department in a tertiary healthcare center. The main outcome measures were change in the acne lesion count, Investigator's Static Global Assessment (ISGA) score, Global Acne Grading System (GAGS) score, and Acne-Specific Quality of Life Questionnaire (Acne-QoL) at the end of 4 weeks of therapy. After randomization one group ($n = 30$) received tazarotene 0.1% plus clindamycin 1% gel and another group ($n = 30$) received adapalene 0.1% plus clindamycin 1% gel for 1 month. At follow-up, all the parameter were reassessed.

Result In both treatment regimens the total number of facial acne lesions decreased significantly. The difference in the change in the total count between the two combination regimens was also significant [6.51, 95% confidence interval (CI) 1.91–11.09, $p = 0.007$]. A $\geq$50% reduction in the total lesion count from the baseline levels was achieved by 71% of patients in the tazarotene plus clindamycin group and 22% of patients in the adapalene plus clindamycin group ($p = 0.0012$). The difference in the change of inflammatory ($p = 0.017$) and non-inflammatory ($p = 0.039$) lesion counts in the tazarotene plus clindamycin group were significantly higher than the adapalene plus clindamycin group. The difference in change of the GAGS score was also significantly higher in the tazarotene plus clindamycin group ($p = 0.003$). The ISGA score improved in 17 patients in the tazarotene plus clindamycin group versusnine patients in the adapalene plus clindamycin group ($p = 0.04$). The change of total quality-of-life score was found to be significantly ($p = 0.027$) higher in the tazarotene plus clindamycin group.

Conclusions Both treatment regimens were efficacious, but tazarotene plus clindamycin was found to be superior to adapalene plus clindamycin. The tolerability profile of both regimens was comparable.

Trial Registration ClinicalTrials.gov Identifier: NCT02721173

✉ Rituparna Maiti
  rituparnamaiti@gmail.com

1 Department of Pharmacology, All India Institute of Medical Sciences (AIIMS), Bhubaneswar, Odisha, India

2 Department of Dermatology, All India Institute of Medical Sciences (AIIMS), Bhubaneswar, Odisha, India

3 All India Institute of Medical Sciences (AIIMS), Bhubaneswar, Odisha, India

4 Institute of Medical Sciences and Sum Hospital, Bhubaneswar, Odisha, India

△ Adis

Key Points

The present study was conducted to compare the efficacy and safety of tazarotene plus clindamycin against adapalene plus clindamycin in facial acne vulgaris.

In this randomized controlled clinical trial on 60 patients with facial acne, tazarotene plus clindamycin showed a better efficacy than adapalene plus clindamycin by decreasing the total number of acne lesions, Global Acne Grading System (GAGS) score, Investigator's Static Global Assessment (ISGA) score, and total Acne-Specific Quality of Life Questionnaire (Acne-QoL) score. The tolerability profile of both regimens was comparable.

This study may help dermatologists choose a better alternative for combination therapy of facial acne.

1 Introduction

Acne vulgaris is one of the most common conditions treated by dermatologists. The pathogenesis of acne is multifactorial, but critical components include abnormal follicular keratinocyte desquamation leading to the formation of a follicular plug (microcomedo), an increase of sebum production within the pilosebaceous follicle, colonization by *Propionibacterium acnes* in the sebum, and inflammation [1–4]. Topical retinoids targeting comedogenesis with anti-inflammatory activity is recommended as first-line therapy for both inflammatory and non-inflammatory acne [5]. The adjuvant use of anti-acne medications can enhance the efficacy of topical retinoid therapy because of their complementary mechanism of action. For example, using clindamycin in conjunction with retinoids has been shown to offer significantly greater efficacy than either topical retinoid alone [6–10]. The adjuvant use of clindamycin has also been shown to decrease the safety issues with topical retinoid therapy [6, 10].

Tazarotene is a synthetic retinoid that has been approved by the US Food and Drug Administration (FDA) for the treatment of acne vulgaris. Tazarotene is a prodrug that is converted to its active form, tazarotenic acid in the skin, which binds to retinoic acid receptors (RARs) and modulates gene transcription through retinoic acid response elements on DNA promoter sites. Tazarotene helps to normalize the abnormal keratinization in the follicular infundibulum and changes the microenvironment of the follicle to reduce the proliferation of *P. acnes* [5].

Adapalene is a synthetic naphthoic acid derivative with retinoid activity. Adapalene acts through RARs and retinoid X receptors (RXRs) and modulates cellular keratinization and the inflammatory process. This anti-inflammatory activity is due to inhibition of the lipoxygenase and the oxidative metabolism of arachidonic acid [11]. Clindamycin is bactericidal to *P. acnes*. Due to the inhibition of *P. acnes*, the free fatty acid levels (a breakdown product of sebum by *P. acnes*) on the skin surface decrease. Topically applied clindamycin phosphate penetrates to a greater extent into open comedones and converts them to sterile comedones [12].

Combination therapy for acne is preferred because it targets multiple steps of acne pathogenesis that could not be accomplished with monotherapy of either active ingredient, thereby improving outcome. A literature review revealed that tazarotene has been compared with adapalene as monotherapy [13, 14], but to date, there has been no comparative study assessing the safety and efficacy of tazarotene plus clindamycin against adapalene plus clindamycin in acne vulgaris. Therefore, the present study has been designed to compare the efficacy and safety of these two combination therapies in patients with facial acne.

2 Patients and Methods

The study was conducted following the Indian Council of Medical Research (ICMR) Ethical Guidelines for Biomedical Research on Human Subjects (2006) after getting the approval of the institutional ethics committee. The study has been registered with ClinicalTrials.gov (identifier: NCT02721173).

2.1 Study Population and Eligibility

Patients aged 12–35 years, of either sex attending the outpatient Dermatology Department of the All India Institute of Medical Sciences (AIIMS), Bhubaneswar (Odisha, India) with facial acne were screened for enrollment in the study. After screening, patients were recruited according to inclusion and exclusion criteria (Table 1).

2.2 Study Design

The present study is a randomized, open-label, active-controlled, parallel-design clinical trial with an allocation ratio of 1:1. Written informed consent was taken from all patients or guardians (for patients below 18 years—assent was taken from these patients) after explaining the diagnosis, the nature, purpose, risk, and benefits of the proposed treatment. After recruitment, a detailed history and clinical evaluations including counting of facial acne lesions,

Table 1 Inclusion and exclusion criteria for recruitment of patients

Inclusion criteria	Exclusion criteria
1. All patients with the diagnosis of facial acne vulgaris with comedones, papules, pustules (≤5), or nodules (≤2) or ISGA score ≤4	1. Very severe acne vulgaris (ISGA score >4)
	2. Any skin disorder that might interfere with the diagnosis or evaluation of acne vulgaris
2. Patients aged 13–35 years, of either sex	3. Known hypersensitivity to retinoids and clindamycin
3. Treatment-naïve patients or patients who had not taken topical anti-acne medications in last 14 days, systemic antibiotics in last 30 days, or oral retinoids in last 12 months	4. Any uncontrolled systemic disease or any cosmetic or surgical procedures complementary to the treatment of acne in the preceding 15 days
	5. Patients who were on oral contraceptive pills in the last 12 weeks
	6. Pregnant and nursing women

ISGA Investigator's Static Global Assessment

Investigator's Static Global Assessment (ISGA) scoring, assessment on the Acne Global Severity Scale, and Acne-Specific Quality of Life Questionnaire (Acne-QoL) scoring were performed at baseline and at the end of therapy. After baseline assessments, recruited patients were randomized by simple randomization into two treatment groups using computer-generated random codes. The random allocation code of the participants was generated by an investigator who was not involved in the patient recruitment. The codes were assigned to a sequence of numbers which was given to another investigator who was responsible for patient recruitment. This process ensured allocation concealment. One group received tazarotene 0.1% gel plus clindamycin 1% gel and the other group received adapalene 0.1% gel plus clindamycin 1% gel. All participants were advised to apply the medications once daily in the evening after facial cleansing. Clindamycin was applied first and the retinoid (tazarotene or adapalene) was applied 10 min later. All patients were followed up for 4 weeks and all outcome parameters were reassessed.

2.3 Efficacy Outcome Measures

2.3.1 Primary Outcome

- Change in the number of facial acne lesions, i.e., total lesion count (inflammatory plus non-inflammatory lesions) at the end of 4 weeks of treatment. Inflammatory lesions include papules, pustules, and nodules, and non-inflammatory lesions include open and closed comedones [15].

2.3.2 Secondary Outcomes

- ISGA score [15]: ISGA is a static assessment of disease status at the time of evaluation. The dermatologic presentation in this score has been categorized into five categories (clear, almost clear, mild, moderate, severe,

very severe) and scoring is on a scale of 0–5 depending on severity.

- Global Acne Grading System (GAGS) score [16, 17]: this system divides the face, chest, and back into six areas (forehead, each cheek, nose, chin and chest, and back) and assigns a factor to each area by size. Each type of lesion is given a value depending on severity: no lesions = 0, comedones = 1, papules = 2, pustules = 3, and nodules = 4. The score for each area (local score) is calculated using the following formula: local score = Factor × Grade (0–4). The global score is the sum of local scores. Acne severity was graded using the obtained global score for the areas included (forehead, cheeks, nose, and chin).

- Acne-QoL [18–20]: the Acne-QoL contains questions organized into four domains which address the impact of facial acne on health-related quality of life. These are self-perception, role-social, role-emotional, and acne symptoms. The items included within each domain are those that the patients consider important. For all domain scores, the responses to items comprising the domain are summed without any weighing scheme.
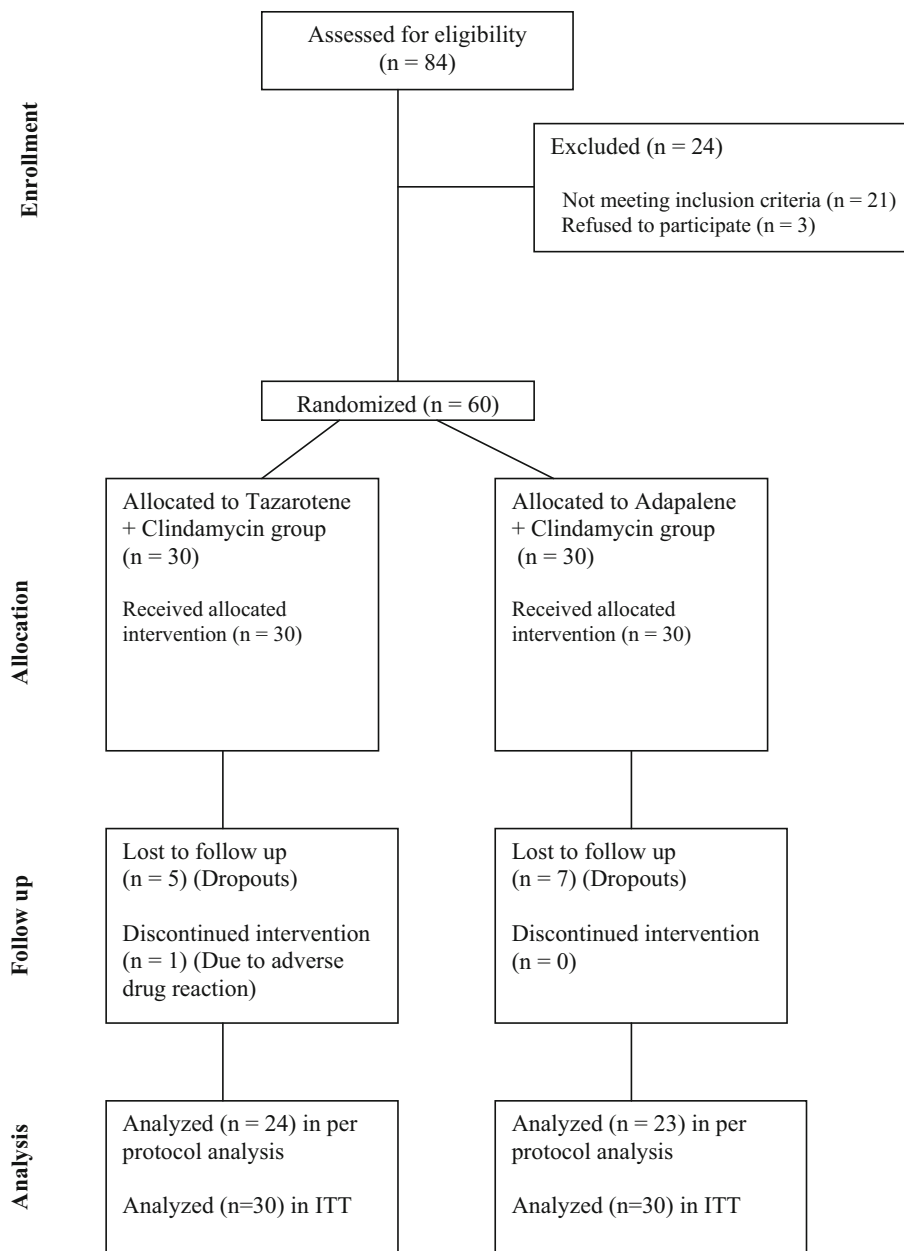
2.4 Safety Measures

Any adverse event (untoward medical occurrence associated with the use of the drug) was sought by non-directive questioning of the patient at the follow-up visit. Patients had free access to the investigators for reporting of any adverse effects experienced by them. Adverse drug reactions were graded into mild, moderate, severe, and life-threatening according to the World Health Organization (WHO) grading scale.

2.5 Statistical Analysis

Continuous variables are represented as mean ± standard deviation and categorical variables as frequency

Fig. 1 CONSORT
(Consolidated Standards Of
Reporting Trials) diagram
showing the flow of participants
through each stage of the
randomized trial. *ITT* intention-
to-treat

Enrollment

Assessed for eligibility
(n = 84)

Excluded (n = 24)

Not meeting inclusion criteria (n = 21)
Refused to participate (n = 3)

Randomized (n = 60)

Allocation

Allocated to Tazarotene
+ Clindamycin group
(n = 30)

Received allocated
intervention (n = 30)

Allocated to Adapalene
+ Clindamycin group
(n = 30)

Received allocated
intervention (n = 30)

Follow up

Lost to follow up
(n = 5) (Dropouts)

Discontinued intervention
(n = 1) (Due to adverse
drug reaction)

Lost to follow up
(n = 7) (Dropouts)

Discontinued intervention
(n = 0)

Analysis

Analyzed (n = 24) in per
protocol analysis

Analyzed (n=30) in ITT

Analyzed (n = 23) in per
protocol analysis

Analyzed (n=30) in ITT

(percentage). Comparison of the means of continuous variables between the groups was made using the unpaired *t* test/Mann–Whitney *U* test and within the group using the two-sided paired *t* test/Wilcoxon matched pair test. Fisher's exact test was used for categorical variables. Both intention-to-treat (ITT) and per-protocol analyses were done. ITT was conducted by replacing missing values using multiple imputation. The imputation was performed five times and the pooled data were used for analysis. Statistical analyses were performed using SPSS® 23.0 statistical software (IBM, New York, NY, USA). A *p* value <0.05 was considered significant. A sample size of 26 in each group was powered at 80% to detect a difference of four in the decrease in the number of total acne lesions between the two groups. The alpha error allowed was 0.05 and the standard deviation was assumed to be five in each group.

3 Results

The recruitment process was started in April 2016 and the study was completed by December 2016. Of 84 facial acne vulgaris patients screened, 24 patients were excluded. Twenty-one patients did not meet the inclusion criteria and another three patients declined to participate. Six patients in the tazarotene plus clindamycin group and seven patients in the adapalene plus clindamycin group were lost to follow-up at the end of treatment period. Of six patients

Table 2 Baseline demographic data and clinical characteristics of the 60 patients with facial acne who participated in the study

Characteristics	Tazarotene + clindamycin group ($n = 30$)	Adapalene + clindamycin group ($n = 30$)	p value[a]
No. of patients recruited	30	30	
No. of patients at follow-up	24	23	
Age (years)	22.1 ± 3.4	21.2 ± 3.8	0.36
Male:female ratio	12:18	14:16	0.79
ISGA score	2 (2–3)	2 (2–2)	0.65
Total acne lesion count	33.93 ± 15.4	30.2 ± 10.6	0.28
Inflammatory lesions	15.2 ± 7.2	14.83 ± 5.7	0.83
Non-inflammatory lesions	18.73 ± 12.7	15.36 ± 8.3	0.23
Global Acne Grading System score	16.06 ± 3.7	16.5 ± 3.0	0.63
Acne-QoL: self-perception	11.76 ± 5.5	14.3 ± 6.7	0.11
Acne-QoL: emotional domain score	10.8 ± 5.4	12.36 ± 6.1	0.30
Acne-QoL: social domain score	11.4 ± 4.7	12.7 ± 5.7	0.34
Acne-QoL: acne symptom domain score	15.06 ± 4.9	14.57 ± 4.9	0.70
Acne-QoL: total score	49.03 ± 15.3	53.97 ± 19.3	0.28

All data are given as mean ± standard deviation, except ISGA score, which is given as median (interquarile range)

Acne-QoL Acne-Specific Quality of Life Questionnaire, *ISGA* Investigator's Static Global Assessment

[a]Unpaired *t* test/Mann–Whitney U test/Fischer's exact test

in the tazarotene plus clindamycin group, one discontinued tazarotene due to a burning sensation that was intolerable for the patient. The reason for the loss of follow-up was not known for the other patients (Fig. 1). There was no significant difference between the groups at baseline (Table 2). Overall, the mean age of the participants was 21.6 years and 56.7% were female.

3.1 Change in Acne Lesion Count

Both groups responded to the treatment as observed in the total lesion count compared to the baseline (Table 3). However, the response in the tazarotene plus clindamycin group was significantly better than the adapalene plus clindamycin group [6.51, 95% confidence interval (CI) 1.91–11.09, $p = 0.007$]. As shown in Table 3, both the inflammatory and non-inflammatory lesions decreased significantly in both groups. The changes in both the inflammatory (3.24, 95% CI 0.59–5.88, $p = 0.017$) and non-inflammatory lesions (3.55, 95% CI 0.18–6.84, $p = 0.039$) were significantly better in the tazarotene plus clindamycin group (Table 3). It was also observed that the tazarotene plus clindamycin group had a significantly higher number of patients who had a reduction of more than 50% of lesions (17) than did the adapalene group (five) ($p = 0.0012$).

3.2 Other Secondary Outcomes

The patients in both groups responded in terms of decrease in GAGS score and ISGA score at the end of 4 weeks.

However, the decrease in these scores in the tazarotene plus clindamycin group was significantly better than in the adapalene plus clindamycin group (Table 3). Seventeen of 24 in the tazarotene plus clindamycin group and nine of 23 in the adapalene plus clindamycin group showed an improvement in ISGA scores. This improvement was better in the tazarotene plus clindamycin group than in the adapalene plusclindamycin group ($p = 0.04$ for Fisher's exact test). In both the groups, all four individual domain scores and the total score for Acne-QoL increased significantly after follow-up. The difference in change of acne symptom domain score (−1.14, 95% CI −2.08 to −1.96, $p = 0.019$) and total score (−2.84, 95% CI −5.34 to −0.34, $p = 0.027$) was significantly better in the tazarotene plus clindamycin group. A similar trend was observed in other domains but was not statistically significant (Table 3).

3.3 Intention-to-Treat Analysis

For ITT analysis, the missing values were replaced using multiple imputation techniques. ITT analysis was performed for outcome measures such as lesion count (both inflammatory and non-inflammatory), GAGS scoring, and Acne-QoL total score. The results were found to be similar to those of per-protocol analysis (Table 4).

3.4 Safety Evaluation

The drug regimens were well-tolerated in both groups. Ten patients from the tazarotene plus clindamycin group and four from the adapalene plus clindamycin group

Table 3 Change in efficacy parameters in study groups over a period of 4 weeks (per-protocol analysis)

Variables	Tazarotene + clindamycin group (n = 24)				Adapalene + clindamycin group (n = 23)				Difference between groups (tazarotene + clindamycin vs. adapalene + clindamycin)	
	First visit	Second visit	Mean difference (95% CI)	p value[b]	First visit	Second visit	Mean difference (95% CI)	p value[b]	Mean difference (95% CI)	p value[c]
Total no. of acne lesion	32.0 ± 13.2	14.46 ± 7.0	17.54 (13.85–21.23)	<0.0001	31.9 ± 11.18	20.87 ± 8.99	11.03 (8.14–13.95)	<0.0001	6.51 (1.91–11.09)	0.007
No. of inflammatory lesions	14.83 ± 7.3	6.29 ± 3.5	8.54 (6.53–10.56)	<0.0001	15.34 ± 6.2	10.04 ± 5.4	5.3 (3.50–7.11)	<0.0001	3.24 (0.59–5.88)	0.017
No. of non-inflammatory lesions	17.17 ± 11.7	7.92 ± 6.3	9.25 (6.07–11.93)	<0.0001	16.56 ± 8.9	10.8 ± 7.5	5.7 (4.07–7.41)	<0.0001	3.55 (0.18–6.84)	0.039
Global Acne Grading System score	16.38 ± 4.0	10.21 ± 3.5	6.17 (5.17–7.16)	<0.0001	16.30 ± 3.3	12.13 ± 3.3	4.17 (3.322–5.025)	<0.0001	2.0 (0.72–5.03)	0.003
ISGA score	2 (2–3)	2 (1–2)		<0.0001	2 (2–2)	2 (2–2)		0.004		0.011
Acne-QoL: self-perception	11.79 ± 5.6	15.46 ± 4.8	−3.36 (−4.29 to −3.05)	<0.0001	13.96 ± 7.3	16.69 ± 6.5	−2.73 (−3.467 to −2.010)	<0.0001	−0.63 (−1.85 to −0.001)	0.050
Acne-QoL: emotional domain score	10.67 ± 5.4	13.70 ± 5.0	−3.03 (−3.80 to −2.28)	<0.0001	10.96 ± 6.0	14.22 ± 5.9	−3.26 (−3.902 to −2.619)	0.0001	−0.22 (0.75–1.19)	0.652
Acne-QoL: social domain score	10.46 ± 4.6	13.5 ± 3.7	−3.04 (−3.87 to −2.21)	0.0001	12.13 ± 6.0	14.17 ± 5.9	−2.04 (−2.702 to −1.385)	0.0001	−1.00 (−2.03 to 0.04)	0.059
Acne-QoL: acne symptom domain score	14.83 ± 4.3	19.7 ± 3.6	−4.87 (−5.69 to −4.07)	<0.0001	13.87 ± 5.3	17.60 ± 4.9	−3.73 (−4.248 to −3.230)	<0.0001	−1.14 (−2.08 to −1.96)	0.019
Acne-QoL: total score	47.75 ± 14.17	62.37 ± 13.6	−14.62 (−16.51 to −12.74)	<0.0001	50.91 ± 20.4	62.69 ± 19.8	−11.78 (−13.52 to −10.05)	<0.0001	−2.84 (−5.34 to −0.34)	0.027

All data are given as mean ± standard deviation, except ISGA score, which is given as median (interquartile range)

Acne-QoL Acne-Specific Quality of Life Questionnaire, *CI* confidence interval, *ISGA* Investigator's Static Global Assessment

[a] Paired *t* test/Wilcoxon matched pair test

[b] Unpaired *t* test/Mann Whitney *U* test

Table 4 Comparative results from per protocol and intention-to-treat analysis

Variables	Tazarotene + clindamycin group		Adapalene + clindamycin group		Difference between groups (tazarotene + clindamycin vs. adapalene + clindamycin)			
	Effect size		Effect size		*p* value		95% CI	
	Per-protocol analysis	ITT	Per-protocol analysis	ITT	Per-protocol analysis	ITT	Per-protocol analysis	ITT
Total no. of acne lesions	17.54	18.01	11.03	10.76	0.007	<0.001	1.91 to 11.09	5.44 to 8.86
No. of inflammatory lesions	8.5	8.6	5.3	5.7	0.017	0.024	0.59 to 5.88	0.37 to 5.28
No. of non-inflammatory lesions	9.25	9.5	5.7	5.8	0.039	0.013	0.18 to 6.84	0.83 to 7.01
Global Acne Grading System score	6.2	6.2	4.17	4.6	0.003	0.033	0.72 to 5.03	0.12 to 2.79
Acne-QoL: total score	−14.62	−13.2	−11.8	−11.9	0.027	0.065	−5.34 to −0.34	−4.79 to 0.15

Acne-QoL Acne-Specific Quality of Life Questionnaire, *CI* confidence interval, *ITT* intention-to-treat

complained of a burning sensation. The severity of burning sensation in 13 patients was mild and tolerable and thus the treatment was continued in those patients. However, one patient on tazarotene plus clindamycin could not tolerate it and the drug was withdrawn. Other than burning sensation, eight patients complained of mild itching and drying of skin. The adverse event profile was statistically similar in both the groups.

4 Discussion

The present study has compared two combination regimens (tazarotene plus clindamycin and adapalene plus clindamycin) for the treatment of acne vulgaris. The two groups were found to be homogenous with respect to baseline demographic and clinical data (Table 2).

The results demonstrate a significant reduction in both the inflammatory and non-inflammatory acne lesions over a period of 4 weeks in both treatment groups. The comparative analysis reveals that the reduction in both inflammatory and non-inflammatory lesions by tazarotene plus clindamycin is superior to adapalene plus clindamycin. This study also reveals the superiority of tazarotene and clindamycin combination using other two efficacy parameters: GAGS score and ISGA score. ITT analysis shows a similar result as per-protocol analysis. A study by Pariser et al. [21] has shown that topical adapalene was non-inferior to tazarotene in total acne result reduction. However, in this study, the retinoids were compared alone rather than in combination with clindamycin. The standard treatment for acne vulgaris is a combination of a retinoid with antimicrobials. The combination is better than either of the agents given as monotherapy. This effect of combination has been proved in various clinical studies [22–24]. Feldman et al.

[15] showed that the average time taken for 50% reduction in the acne lesions with tazarotene alone was 57 days, but in our study 71% of the patients in the tazarotene group had ≥50% reduction in the total lesion count at the end of 4 weeks. This might be due to the addition of clindamycin with tazarotene. It has been discussed that, apart from thinning the stratum corneum, retinoids indirectly inhibit the bacteria by altering the follicular milieu [5]. Moreover, retinoids also improve the phagocytic function of macrophages, thereby positively interacting with clindamycin in eliminating the causative bacteria [25]. This finding in our study suggests a possibility of synergism between tazarotene and antibiotics. However, in the case of adapalene and clindamycin combination, 50% reduction at 4 weeks was observed in only 22% of patients, which was significantly less than with tazarotene plus clindamycin. This difference in pharmacodynamic interaction could be explored in future clinical trials. It has also been discussed that adapalene binds to RARs and then the complex binds with RXRs [11], whereas tazarotenic acid (the active form of tazarotene) does not bind to RXRs and selectively binds with RARs [5]. This might explain the difference in the clinical outcomes between the two drugs, which have to be experimentally verified. Among all four domains of Acne-QoL, the change in symptom domain score in the tazarotene plus clindamycin group was found to be significantly higher than for adapalene, suggesting better symptomatic improvement in the tazarotene plus clindamycin group. In other domains such as self-perception and the social and emotional domains, both combination regimens improved the scores significantly from baseline but the mean changes in the tazarotene plus clindamycin group were not significantly different from adapalene plus clindamycin.

This study demonstrated a similar tolerability profile in both the groups even though there was a greater number of adverse

events with tazarotene plus clindamycin. This might be due to a lesser sample size that was not powered enough to detect a significant difference in the adverse events between the groups. Observations of the present study regarding tolerability are similar to the findings in another study by Pariser et al. [21]. The mechanisms of the anti-inflammatory properties exhibited by both drugs are different at the molecular level and the localization of adapalene to the epidermis might explain the subtle difference in the risk of adverse drug reactions between the two drugs [26]. Overall, both regimens were well-tolerated in both groups. This is similar to the study by Tanghetti et al. [22], which found that both retinoid and clindamycin regimens were tolerated well with respect to dryness, erythema, peeling, burning, pruritus, and perception of oiliness.

The limitations of the study are its non-blinded design, smaller sample size, and a relatively short follow-up period.

5 Conclusion

Tazarotene plus clindamycin offers a significantly better efficacy than adapalene plus clindamycin when used once daily to treat facial acne vulgaris. Both combination regimens (tazarotene plus clindamycin and adapalene plus clindamycin) were similarly well-tolerated, though more adverse events were reported with the tazarotene plus clindamycin regimen.

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