

Original Article

Effect of Application, Duration and Dosing Frequency on the Efficacy and Adverse Effect of Adapalene in Acne Vulgaris: an Open-Label Randomized Controlled Study

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ABSTRACT

Introduction: Topical retinoids are the mainstay of treatment for mild and moderate acne but longer duration of application causes adverse effects. The study aimed to evaluate the effect of application, duration and dosing frequency on the efficacy and adverse effect of Adapalene in Acne Vulgaris.

Materials and Methods: The study design was an open-label randomized controlled split-face trial. Patients with acne grades 1 and 2 were randomized into three groups using the split-face technique on the right and left sides. On the right side, patients applied adapalene daily in all the groups and alternately on the left face. The three groups of the study were overnight, 1 hour, and ½ hour application of adapalene. Follow up period was 4,8 and 12 weeks. Lesion count and side effects were evaluated at each follow-up.

Results: Out of 292 who completed the study, the decrease in total lesion count was highest in the overnight group. Regarding specific lesion count, the decrease in non-inflammatory lesions was highest in the overnight group. However, short contact therapy with 1-hour application showed comparable efficacy with the overnight group in regards to inflammatory lesion count. There was a significant reduction of lesions in all groups from baseline to 12 weeks, with ½ hour group having minimal side effects followed by 1 hour and overnight.

Conclusion: Short contact therapy of acne shows promising results in regard to efficacy and better tolerance.

Keywords: Acne vulgaris; Adapalene; Short contact therapy

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INTRODUCTION

Acne vulgaris is a chronic inflammatory condition of the pilosebaceous unit that affects seborrheic areas such as the face, chest, and back. It is distinguished by comedones, papules, pustules, nodules, cysts, and scars. There are various types of acne-like acne (A) Vulgaris, A. Mechanica, A. fulminant, A. Cosmetic, and A. Rosacea. Acne can be divided into two major groups, inflammatory which includes nodules, pustules, and papules, and non-inflammatory which are open and closed comedones.¹ The 2010 global burden of disease report showed that acne vulgaris is the eighth most severe skin condition with an overall global incidence of 9.38 percent (for all ages) and about 85 percent of young adults are affected by acne vulgaris between the ages of 12 and 25 years.² The pathogenesis of acne is multifactorial and includes four primary pathogenic factors: (a) an inflammatory reaction triggered by Propionibacterium acnes, (b) bacterial proliferation and colonization of the duct, most commonly Propionibacterium acnes, while no strong proof of a causal association between Propionibacterium acnes and acne vulgaris is available (c) a rise in the development of sebum from the swollen sebaceous gland owing to increased androgen content; and (d) abnormal pilosebaceous hyperkeratinisation with the formation of comedones caused by enhanced androgens.³ The topical retinoids result in the reduced proliferation of skin cells and keratinization. Adapalene is a derivative of naphthoic acid and it is a third-generation retinoid, with anti-inflammatory, anti-comedogenic, and comedolytic properties. The retinoids play a major role in the in-regulation of desquamation at keratinocytes, resulting in comedolysis and the abolition of new microcomedonal growth. Topical retinoids are used in non-inflammatory acne as a monotherapy and in conjunction with certain topical drugs in inflammatory and more extreme types of acne.⁴ The adverse effects of retinoids, which includes stinging, itching, dryness, and erythema, often arise during the early stages of treatment. The study aimed to evaluate the effect of application, duration and dosing frequency on the efficacy and adverse effect of Adapalene in Acne Vulgaris

MATERIALS AND METHODS

The study design was an open-label randomized controlled split-face trial. The study was conducted from April 2019 to March 2020 at a tertiary health care centre. Ethical approval was taken from Institute Ethical Committee and registered with the clinical trial registry of India (CTRI/2019/03/018222). The enrolled subjects were patients of acne grade 1 and II (Global Investigator Assessment Scale for Acne Vulgaris) attending Dermatology and Venereology outpatient department. Only topical treatment was given to all patients. The inclusion criteria were age between 13 to 40 years, acne grade 1 and II, and patients not using any topical preparation for the last month. Exclusion criteria were pregnant and breastfeeding women, patients with hypersensitivity to adapalene, patients not giving informed consent, uncooperative patients, patients undergoing frequent facial procedures, and patients with a history of any oral drug intake like steroids, anticonvulsants, antipsychotics, anti-inflammatory, antibiotics, oral contraceptive pills, lithium, etc. for last three months. The

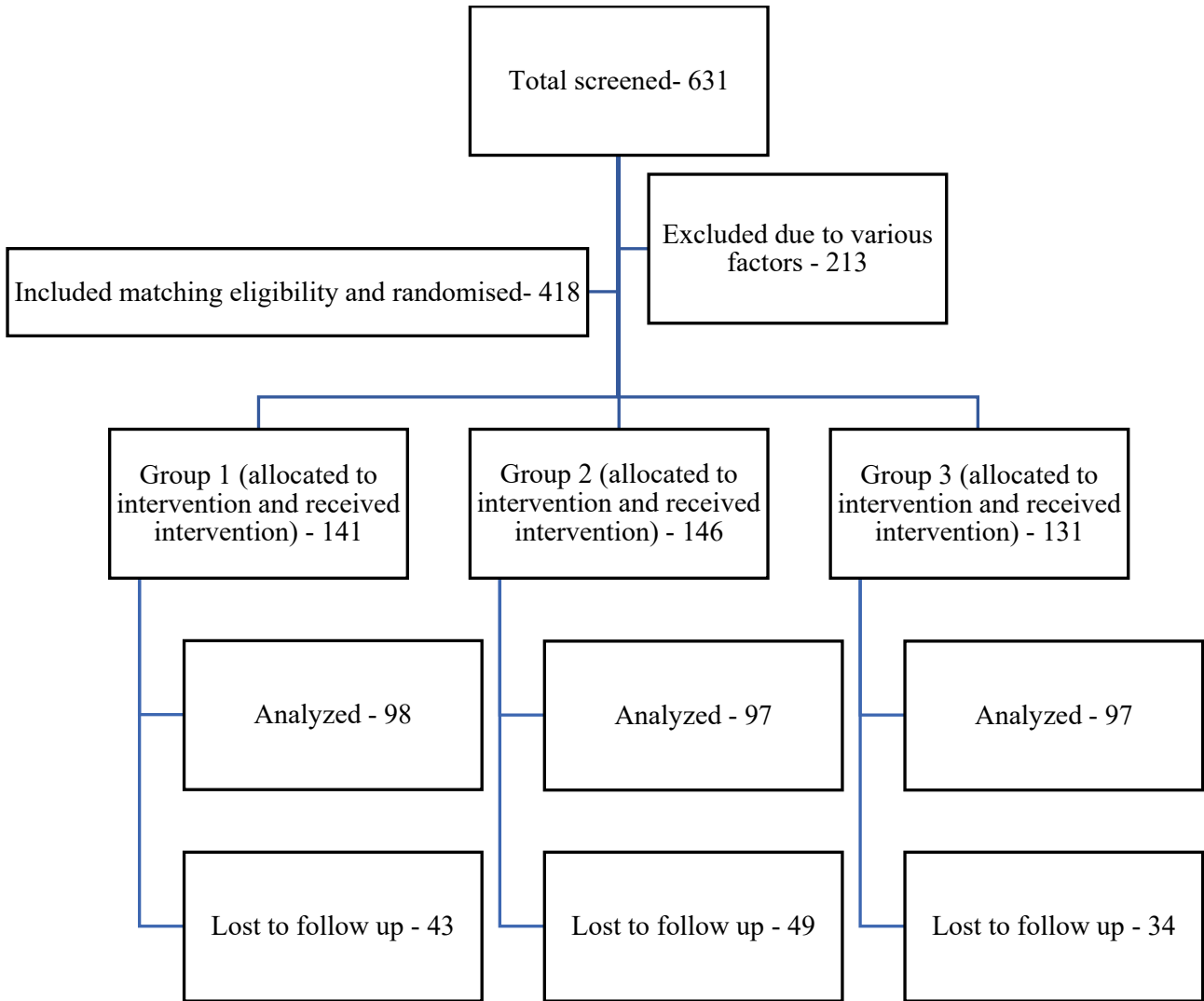
allocation of subjects in three treatment regimens was done through computer-generated randomisation. In each group, the face was divided anatomically into two parts for study by a vertical line passing through the nasal septum. In all the groups, a daily application was given on the right side and an alternate day on the left side. In Group 1: overnight application group. Group 2: one-hour application and Group 3: half an hour application. The endpoint of the study was 12 weeks. Patients were advised to apply 0.1 percent adapalene gel. Patients were asked to wipe gently with cotton thrice to clean the applied medicine after a specific duration of adapalene application. Patients were evaluated at baseline, 4, 8, and 12 weeks. Counting of total lesions and specific lesions (comedones, papules, and pustules) on each side. Assessment of side effects like burning, itching, and scaling as well as the measurement of clinical erythema assessment (CEA) for erythema was done at each follow-up. The CEA scale explains the erythema in the five severity grades (0 to 4). Grade 0: Clear, no signs, Grade 1: Almost clear, slight red, Grade 2: Mild, definite redness, Grade 3: Moderate redness and Grade 4: Severe, fiery redness. Investigator global scale was used for acne grading at baseline for inclusion and exclusion. It was not measured during follow-up because Acne grading relies on the whole face rather than half face.

The sample size was calculated by the following formula using the level of significance $p < 0.05$ and 80% power of the study. The calculated sample size will be 291. Further assuming 20% loss to follow up during treatment, $N = n/1-d$ ($d=0.2$). Therefore, the final sample size for randomization would be $291/(1-0.2) = 364$.

Data analysis was done using STATA and SPSS 22.0 trial version. Student's t-test was used for the analysis of the mean reduction of a total lesion at the end point from baseline, Anova Tukey-HSD test for analysis of mean (total lesion count) between intergroup, univariate analysis for specific lesion count comparison between groups, multivariate analysis for specific lesion count comparison between groups to adjust for age, sex, and baseline count. Poisson's regression analysis is used for comparison of left face vs right face, ordered logistic regression for CEA – [data presented as IRR (Incidence rate ratio), mean percentage (%) reduction for total lesion count, 95% confidence interval and p value < 0.05 was taken as significant value]. For the spectrum of side effect comparison between groups, the chi-square test was used.

RESULTS

A total of 631 patients were screened and 418 were included and randomized. Two hundred ninety-two patients completed the study (flow chart 1).



The basic characteristics of patients are summarized in Table 1.

Mean reduction in total lesion count of 84.39% and 81.23% for the right and left side of the overnight group respectively was found to be highest in comparison to other groups (table 1; fig. 1). In intergroup comparison, there was a significant reduction in the overnight group compared to ½-hour groups, however with the 1-hour group, it was not significant. There is a significant decrease in lesion count with one-hour application compared to ½-hour on both sides.

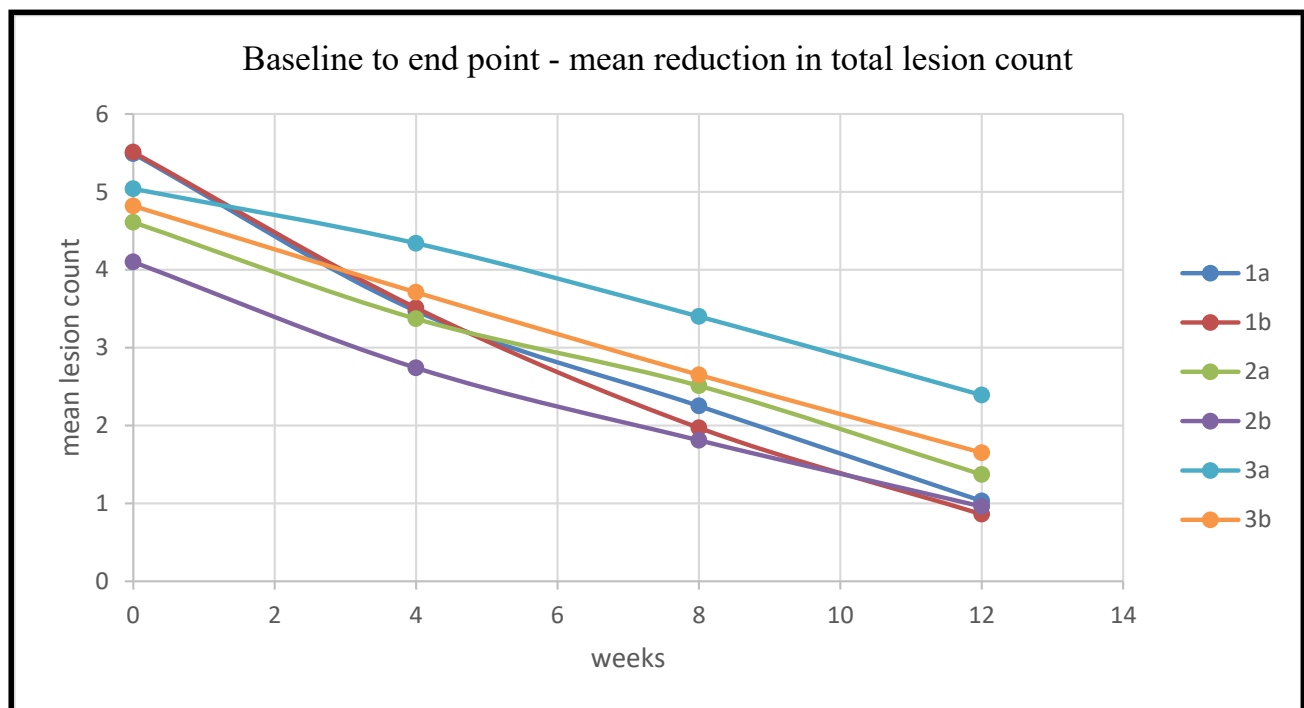
Table 1: Demonstration of basic characteristics of patients

Total number of patients (Contd..)		292
Sex	Female	184 (63.01%)
	Male	108 (36.99%)
Age (years)	Range	13-40
	Mean ± SD	25.08 ± 6.14

Total number of patients (Contd..)		292
Occupation	Professional	74 (25.34%)
	Non-professional	103 (35.27%)
	Student	115 (39.38%)
Total duration (months)	Range	0.23-36
	Mean ± SD	4.41 ± 4.18
Education	High school	174 (59.59%)
	Intermediate	66 (22.60%)
	Graduate	37 (12.67%)
	Post-graduate	15 (5.14%)
Baseline Acne grade	Acne grade I	128 (43.83%)
	Acne grade II	164 (56.16%)

Table 2: Inter and intra-group comparison of mean reduction in total lesion count

GROUP	Baseline M0 ± SD0	Mean ± (SD)			t test (M0-M3)	% mean reduction (M0-M3)	Anova F – Tukey HSD Test (Mean) Inter split face comparison	
		4 weeks M1 ± SD1	8 weeks M2 ± SD2	End point M3 ± SD3				
Overnight left (1a)	5.49±5.82	3.47±4.02 M0 – M1 p<0.05	2.25±2.87 M0-M2 p<0.05	1.03 ±1.48	p<0.05	81.23	1b vs 1a: p=0.2 1a vs 2b: p=0.34	1a vs 1b vs 2b p=0.27, F=1.28
Overnight right (1b)	5.51±5.59	3.51±3.68 M0-M1 p<0.05	1.97±2.24 M0-M2 p<0.05	0.86±1.26	p<0.05	84.39	1b vs 2b: p=0.2 1a vs 3b: p<0.01	1a vs 2a vs 2b p<0.01 F=4.86
1-hour left (2a)	4.61±7.18	3.37±5.47 M0-M1 p<0.05	2.51±4.52 M0-M2 P<0.05	1.37±2.64	p<0.05	70.28	1b vs 2a: p<0.01 1a vs 2a: p=0.1	1b vs 2a vs 2b p<0.001 F=7.74
1-hour right (2b)	4.10±6.35	2.74±4.62 MO-M1 p<0.05	1.81±3.29 M0-M2 p<0.05	0.96±1.84	p<0.05	76.58	2a vs 2b: p<0.01 2b vs 3a: p<0.01	2a vs 3a vs 3b p<0.01 F=12.7
½-hour left (3a)	5.04±6.14	4.34±5.59 M0-M1 p<0.05	3.40±4.69 M0-M2 p<0.05	2.39±3.58	p<0.05	52.57	2a vs 3b: p=0.3 2b vs 3a: p<0.01	2b vs 3a vs 3b p<0.001 F=27.3
½-hour right (3b)	4.82±5.68	3.71±4.64 M0-M1 p<0.05	2.65±3.58 M0-M2 p<0.05	1.65±2.39	p<0.05	65.76	3a vs 3b: p<0.01 2b vs 3b: p<0.01	

**Figure 1: Line graph representing a mean reduction in total lesion count of all groups from baseline to 12 weeks.**

Overnight application of adapalene on both sides of the face was superior to both 1-hour and ½-hour applications for open comedones at 12 weeks (Table 3). For closed comedones on both sides, the overnight group had similar efficacy to the 1-hour group. Overnight and 1-hour were superior to ½-hour on both sides. A decrease in papules count in 1-hour and ½ hour groups are comparable to overnight for both sides in the daily application group but the response was less with ½ hour alternate day application. Comparable efficacy was found for pustules with overnight and the other two groups except for ½-hour alternate application, in which it was less effective compared to overnight and 1-hour group (Table 3).

Table 3: Comparison of specific lesion count using univariate analysis

Overnight comparison group	LEFT						RIGHT					
	4 weeks		8 weeks		12 weeks		4 weeks		8 weeks		12 weeks	
	IRR (CI)	P	IRR (CI)	p	IRR (CI)	p	IRR (CI)	p	IRR (CI)	p	IRR (CI)	P
OPEN COMEDONES												
1 hour	1.24 (1.23 – 1.38)	0.001	1.43 (1.27 – 1.61)	0.001	1.8 (1.51 – 2.13)	0.001	1.26 (1.13 – 1.42)	0.001	1.58 (1.36 – 1.83)	0.001	1.98 (1.6 – 2.45)	0.001
Half hour	1.34 (1.21 – 1.49)	0.001	1.62 (1.44 – 1.81)	0.001	3.02 (2.57 – 3.53)	0.001	1.44 (1.29 – 1.61)	0.001	2 (1.75 – 2.32)	0.001	2.91 (2.38 – 3.55)	0.001
CLOSED COMEDONES												
1 hour	0.85 (0.74 – 0.98)	0.02	0.97 (0.82 – 1.14)	0.67	1.13 (0.9 – 1.43)	0.3	0.75 (0.65 – 0.87)	0.001	0.96 (0.8 – 1.14)	0.63	0.95 (0.73 – 1.23)	0.7
Half hour	1.18 (1.04 – 1.34)	0.008	1.48 (1.28 – 1.72)	0.001	2.09 (1.7 – 2.57)	0.001	0.98 (0.86 – 1.12)	0.77	1.27 (1.08 – 1.5)	0.005	1.54 (1.22 – 1.95)	0.001
PAPULES												
1 hour	0.37 (0.27 – 0.51)	0.001	0.26 (0.16 – 0.42)	0.001	0.26 (0.13 – 0.53)	0.001	0.1 (0.07 – 0.15)	0.001	0.04 (0.02 – 0.08)	0.001	0.02 (0.004 – 0.07)	0.001
Half hour	0.67 (0.51 – 0.87)	0.005	0.68 (0.47 – 0.98)	0.04	1.13 (0.66 – 1.94)	0.65	0.4 (0.31 – 0.52)	0.001	0.45 (0.32 – 0.63)	0.001	0.43 (0.29 – 0.66)	0.001
PUSTULES												
1 hour	0.45 (0.3 – 0.68)	0.001	0.54 (0.31 – 0.94)	0.03	0.5 (0.18 – 1.45)	0.21	0.32 (0.21 – 0.5)	0.001	0.29 (0.16 – 0.54)	0.001	0.23 (0.08 – 0.68)	0.008
Half hour	1.52 (1.08 – 2.16)	0.02	1.75 (1.05 – 2.89)	0.03	6.96 (4.12 – 11.74)	0.001	0.95 (0.67 – 1.33)	0.76	1.24 (0.72 – 2.14)	0.45	1.08 (0.36 – 3.26)	0.89

There was a significant reduction of open and closed comedones (non – inflammatory lesions) at 12 weeks for the overnight group on both sides compared to the other two groups adjusting to age, sex, and baseline comedones count (Table 4).

Comparable efficacy was found for inflammatory lesions (papules and pustules) overnight and in the other two groups. The lesion count was significantly reduced with daily application across all groups. Similar efficacy was found in inflammatory lesions for the overnight group on both sides (Table 5).

Table 4: Comparison of specific lesions between sides

Overnight comparison group	LEFT						RIGHT					
	4 weeks		8 weeks		12 weeks		4 weeks		8 weeks		12 weeks	
	IRR (CI)	p	IRR (CI)	p	IRR (CI)	p	IRR (CI)	p	IRR (CI)	p	IRR (CI)	P
OPEN COMEDONES												
1 hour	0.95 (0.85 – 1.05)	0.3	1.08 (0.95 – 1.22)	0.2	1.22 (1.02 – 1.46)	0.03	0.99 (0.89 – 1.12)	0.97	1.25 (1.07 – 1.45)	0.004	1.59 (1.28 – 1.97)	0.001
Half hour	1.26 (1.14 – 1.4)	0.001	1.52 (1.35 – 1.71)	0.001	2.68 (2.28 – 3.14)	0.001	1.2 (1.07 – 1.35)	0.002	1.68 (1.45 – 1.95)	0.001	2.46 (2 – 3.03)	0.001
CLOSED COMEDONES												
1 hour	1.06 (0.93 – 1.22)	0.38	1.21 (1.02 – 1.43)	0.03	1.45 (1.14 – 1.84)	0.002	1.09 (0.94 – 1.27)	0.24	1.44 (1.19 – 1.74)	0.001	1.43 (1.08 – 1.89)	0.01
Half hour	1.25 (1.1 – 1.43)	0.001	1.56 (1.33 – 1.82)	0.001	2.26 (1.82 – 2.8)	0.001	1.65 (1.42 – 1.91)	0.001	2.23 (1.84 – 2.69)	0.001	2.65 (2.02 – 3.47)	0.001
PAPULES												
1 hour	0.59 (0.44 – 0.79)	0.001	0.44 (0.28 – 0.69)	0.001	0.5 (0.25 – 0.98)	0.04	0.19 (0.07 – 0.51)	0.001	0.13 (0.06 – 0.3)	0.001	0.16 (0.03 – 0.76)	0.02
Half hour	0.85 (0.67 – 1.07)	0.17	0.69 (0.5 – 0.95)	0.02	0.92 (0.59 – 1.43)	0.7	0.84 (0.61 – 1.15)	0.28	0.5 (0.38 – 0.66)	0.001	0.76 (0.5 – 1.14)	0.2
PUSTULES												
1 hour	0.82 (0.56 – 1.21)	0.32	1.12 (0.68 – 1.85)	0.66	1.16 (0.54 – 2.5)	0.7	0.83 (0.54 – 1.27)	0.39	0.68 (0.38 – 1.25)	0.22	1.04 (0.39 – 2.73)	0.94
Half hour	1.35 (1.02 – 1.78)	0.04	1.42 (0.98 – 2.06)	0.07	2.54 (1.47 – 4.37)	0.001	0.93 (0.7 – 1.23)	0.6	0.84 (0.58 – 1.23)	0.38	1.58 (0.86 – 2.92)	0.14

Table 5: Comparison of specific lesion count using multivariate analysis

	IRR (CI) 4 weeks	p-value	IRR (CI) 8 weeks	p-value	IRR (CI) 12 weeks	p-value
Open comedones						
Overnight	0.81 (0.72 – 0.91)	0.001	0.63 (0.54 – 0.73)	0.001	0.63 (0.5 – 0.78)	0.001
1- hour	0.83 (0.75 – 0.92)	0.001	0.7 (0.62 – 0.79)	0.001	0.7 (0.6 – 0.82)	0.001
Half an hour	0.87 (0.79 – 0.96)	0.007	0.79 (0.71 – 0.88)	0.001	0.61 (0.54 – 0.7)	0.001
Closed comedones						
Overnight	0.98 (0.86 – 1.11)	0.71	0.86 (0.72 – 1.01)	0.07	0.86 (0.69 – 1.1)	0.23
1- hour	0.86 (0.74 – 0.998)	0.048	0.85 (0.71 – 1.009)	0.064	0.72 (0.56 – 0.92)	0.009
Half an hour	0.81 (0.71 – 0.92)	0.00	0.73 (0.63 – 0.85)	0.001	0.63 (0.52 – 0.76)	0.001
Papules						
Overnight	1.65 (1.35 – 2.04)	0.001	1.31 (0.97 – 1.76)	0.08	1.13 (0.65 – 1.97)	0.67
1- hour	0.39 (0.24 – 0.66)	0.001	0.11 (0.04 – 0.3)	0.001	0.14 (0.03 – 0.63)	0.01
Half an hour	1 (0.73 – 1.36)	0.99	0.87 (0.58 – 1.32)	0.51	0.43 (0.23 – 0.83)	0.01
Pustules						
Overnight	1.1 (0.73 – 1.64)	0.66	0.8 (0.41 – 1.56)	0.51	6.3 (0.76 – 52.5)	0.09
1- hour	1.71 (0.84 – 3.49)	0.14	1.36 (0.5 – 3.67)	0.54	0.55 (0.2 – 1.47)	0.23
Half an hour	0.62 (0.44 – 0.88)	0.008	0.57 (0.35 – 0.94)	0.03	0.34 (0.16 – 0.71)	0.004

The frequency of CEA grading in each follow-up is demonstrated in Table 6. A comparison of CEA is demonstrated in Table 7. The right face had more grade 1 and 2 CEA compared to the left face at 4 weeks in the overnight group ($P=0.01$), however, no significant difference was detected between the right and left sides of the face in the 1-hour ($P=0.15$) and the half-hour ($P=0.3$) groups.

Table 6: Representing CEA frequency with the timeline

	Left face			Right face		
	Overnight	1-hour	Half hour	Overnight	1-hour	Half hour
Grade 0	98	97	97	98	97	97
Grade 1	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0
4 weeks						
Grade 0	81	86	94	65	79	91
Grade 1	12	11	3	26	16	5
Grade 2	5	0	0	7	2	1
Grade 3	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0
8 weeks						
Grade 0	94	97	97	85	97	97
Grade 1	3	0	0	10	0	0
Grade 2	1	0	0	2	0	0
Grade 3	0	0	0	1	0	0
Grade 4	0	0	0	0	0	0
12 weeks						
Grade 0	97	97	97	96	97	97
Grade 1	0	0	0	1	0	0
Grade 2	1	0	0	1	0	0
Grade 3	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0

Table 7: Comparison of CEA between groups and between sides.

Group	Left face - 4 weeks OR (CI)	p-value
Overnight	COMPARISON GROUP	
1 hour	0.58 (0.26 – 1.31)	0.19
Half hour	0.15 (0.04 – 0.52)	0.003*
	Right face - 4 weeks	
Overnight	COMPARISON GROUP	
1 hour	0.44 (0.23 – 0.85)	0.01
Half hour	0.13 (0.05 – 0.32)	0.001
	Overnight – 4 weeks	
Group	OR (CI)	p-value
Left	COMPARISON GROUP	
Right	2.33 (1.2 – 4.5)	0.01
	1-hour – 4 weeks	
Right	1.81 (0.81 – 4.07)	0.15
	Half hour – 4 weeks	
Right	2.08 (0.5 – 8.57)	0.3

The frequency of side effects - burning, scaling, and itching and their comparison are mentioned in Table 8. The bar diagram representing the frequency of patients experiencing side effects is represented in Figures 2a, 2b and 2c.

Adverse effects (Frequency)	GROUP 1		GROUP 2		GROUP 3	
	Right	Left	Right	Left	Right	Left
Burning	28	16	14	12	4	2
Itching	32	18	18	12	3	1
Scaling	12	9	8	5	1	0

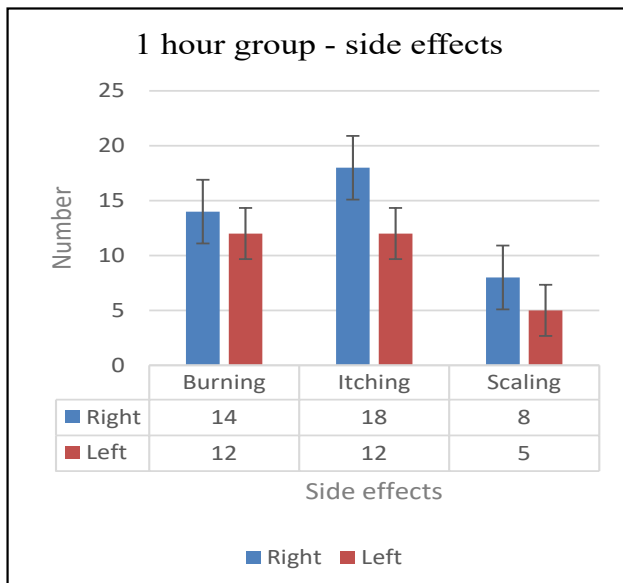
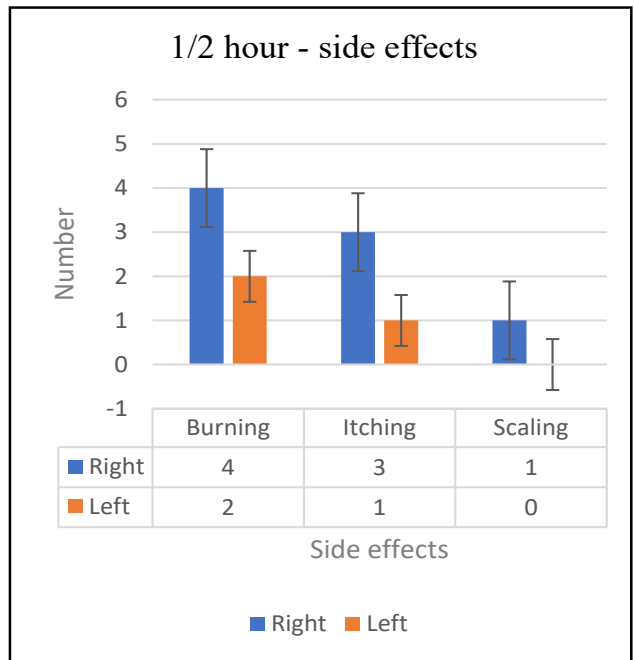
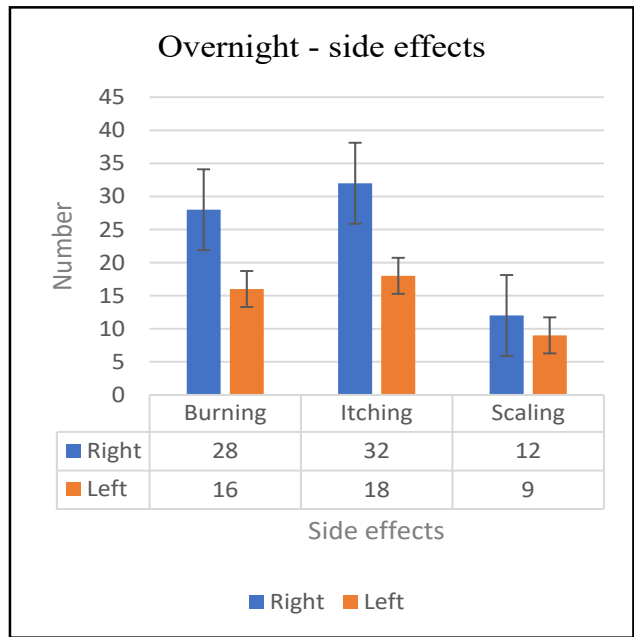


Figure 2a, 2b, and 2c: Bar diagram representing frequency spectrum of side effects across groups

DISCUSSION

Patients with acne had higher rates of unemployment and lower academic performance relative to people without acne. Acne can negatively impact interpersonal relationships, mood, and self-esteem among young adults.⁵ Topical retinoid remains the most clinically efficient anti-acne medication, the cause being a multimodal intervention in regulating the causes that trigger acne. In this study, the papules, pustules, open comedones, and closed comedones treated by adapalene showed a significant reduction of symptoms at 4 to 12 weeks duration. Our study findings are similar to the previous study by Nyirady et al.⁶ who demonstrated that a greater decrease in comedones numbers was found in

patients treated with adapalene gel and tretinoin gel at 2 to 12 weeks duration.

There has been no study on efficacy and comparison of side effects of short contact therapy (SCT) with different groups in acne vulgaris, which necessitates the need for our study due to overnight retinoid application being commonly associated with adverse effects which leads to a loss in follow up and non-treatment adherence. In one of the systematic reviews, "fear of adverse reaction" was categorized under primary non-adherence hurdles, and "adverse reaction" was categorized under secondary non-adherence hurdles to treatment.⁷ Therefore, adverse effects are a vital aspect often ignored while treating acne. In our study, patients in the overnight group demonstrated more side effects compared to 1-hour application followed by ½-hour. Half an hour group demonstrated the least adverse effects of them all ($P < 0.001$). Although, short contact therapy with adapalene is beneficial in adherence response to treatment was less compared with the overnight application. Short contact therapy with topical steroids has been proven beneficial in skin conditions like psoriasis.⁸

There has been a single study of SCT conducted on topical retinoids in the treatment of acne vulgaris which showed similar results to our study in relation to adverse effects, although no comparison of specific lesions with other groups was done. Tretinoin was used as short contact therapy (SCT) in mild to moderate acne. It was a non-funded, pilot, open, multicenter study. Seventy-four patients were treated with 0.05% tretinoin cream which was applied once daily for ½-hour. Treatment duration was from 8 to 32 weeks with a mean duration of 3 months. Thirteen patients (17.6%) developed mild skin irritation and four patients (5.4%) stopped the treatment because of severe adverse effects. The authors evaluated acne severity and treatment efficacy by means of the Global Acne Grading System. Significant clinical improvement ($\geq 50\%$ from baseline) was observed in 41 patients (55.4%).⁹

In our study, for ½-hour daily application of adapalene leads to side effects of 8.25%. Similarly, side effects were 3.1% for ½-hour

alternate, 41.24% in 1-hour daily, 29.90% in 1-hour alternate, 73.47% in overnight daily, and 43.88% in overnight alternate day application. Therefore, SCT seems to be superimposable to that of tretinoin used according to standard modality. The tolerability of SCT with adapalene is very good. This tolerability allows a high adherence of patients to the treatment and it markedly improves compliance. The mean reduction in total lesion count at end of the study was 84.39% for overnight daily, 81.23% for overnight alternate, 76.58% for 1-hour daily, 70.28% for 1-hour alternate, 65.76% for ½-hour daily and 56.27% for ½-hour alternate day application.

We demonstrated good efficacy of SCT in regards to inflammatory lesion count (papules and pustules) which was comparable to the overnight group. We also found similar efficacy of the 1-hour group of left and right application compared to both sides of overnight treatment, in the case of non-inflammatory closed comedones. Therefore, it further supports our study regarding the efficacy of SCT of adapalene gel.

LIMITATIONS

The limitations of our study include a short follow of the time period and no comparison was done with a vehicle in the gel.

CONCLUSIONS

Short contact therapy (SCT) of adapalene has shown similar efficacy in inflammatory lesion count (papules and pustules) as compared to the overnight group. Comparable efficacy was found with the 1-hour group in regards to non-inflammatory (closed comedones) with the overnight group. A significant reduction of total lesion count with short contact therapy with negligible side effects was found which will increase adherence to therapy. The potential role of SCT in future therapy modalities for acne vulgaris should be considered.

REFERENCES

1. AK Mohiuddin. A Comprehensive Review of Acne Vulgaris. Clin Res Dermatology Open Access. 2019;6:1-34. [Crossref](#)
2. Heng AHS, Chew FT. Systematic review of the epidemiology of acne vulgaris. Sci Rep. 2020 Apr 1;10(1):5754. [Crossref](#)
3. Kim SY, Ochsendorf FR. New developments in acne treatment: role of combination adapalene benzoylperoxide. Ther Clin Risk Manag. 2016;12:1497-506. [Crossref](#)
4. Sacchidanand SA, Lahiri K, Godse K, et al. Synchronizing pharmacotherapy in acne with review of clinical care. Indian J Dermatol. 2017;62:341-57. [Crossref](#)
5. Durai PT, Nair DG. Acne vulgaris and quality of life among young adults in South India. Indian J Dermatol 2015;60:33-40. [Crossref](#)
6. Nighland NM, Berger R, Jorizzo J, et al. A comparative trial of two retinoids commonly used in the treatment of acne vulgaris. J Dermatolog Treat. 2001;12:149-57. [Crossref](#)
7. Moradi Tuchayi S, Alexander TM, Nadkarni A, et al. Interventions to increase adherence to acne treatment. Patient Prefer Adherence. 2016;10:2091-6. [Crossref](#)
8. Singh S, Singh SK, Pandey SS. Effect of duration of application and dosing frequency on the efficacy of topical 0.1% mometasone furoate ointment in psoriasis. J Dermatol Treat 1998;9:25-30. [Crossref](#)
9. Veraldi, S., Barbareschi, M., Benardon, S., et al. Short contact therapy of acne with tretinoin. The Journal of dermatological treatment, 2013;24: 374-6. [Crossref](#)