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Research Article

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A comparative study of efficacy and safety of combination of topical 1% clindamycin and 0.1% adapalene with 1% clindamycin and 2.5% benzoyl peroxide in mild to moderate acne at a tertiary care hospital

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ABSTRACT

Acne vulgaris is a very common skin disorder and topical combination therapy in acne produces greater and faster results, minimizes adverse effects and improves compliance. The objective of this study was to compare the efficacy and safety of combination of topical 1% clindamycin and 0.1% adapalene with combination of topical 1% clindamycin and 2.5% benzoyl peroxide in mild to moderate acne vulgaris. Our study was done on 120 patients diagnosed with mild to moderate acne on face (as per Indian Acne Alliance grading for severity of acne). They were randomly assigned into 2 groups (A and B) of 60 each, group A having received combination of topical 1% clindamycin and 0.1% adapalene while group B having received combination of topical 1% clindamycin and 2.5% benzoyl peroxide once daily at night for 12 weeks. Efficacy assessment was done by comparing acne lesion counts at follow ups with their baseline lesion counts [total, noninflammatory and inflammatory acne lesion counts] and safety assessment was done to determine the comparative local and systemic tolerability at the end of 4, 8 and 12 weeks. Significantly greater reduction in mean percentage of total (-0.70±0.05 vs -0.51±0.03), noninfl ammatory (-0.68±0.07 vs -0.49±0.03) and inflammatory (-0.77±0 .06 vs -0.57±0.06) acne lesion counts was seen in group A than group B at 12 weeks, (P < 0.001 - for all types of acne lesion counts). Group A was better tolerated than group B with less irritation (52.5%vs 72.4%, P < 0.027). Thus, we conclude that the combination of topical 1% clindamycin and 0.1% adapalene is superior to combination of topical 1% clindamycin and 2.5% benzoyl peroxide in the treatment of mild to moderate acne vulgaris.

Key words: Acne vulgaris; clindamycin 1%; adapalene 0.1%; benzoyl peroxide 2.5%; meta-analysis and acne

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INTRODUCTION

Acne is a chronic inflammatory disease of pilosebaceous unit. Prevalence being 56% in boys and 45% in girls between 14 to 16 years of age group [1]. Acne affecting on face results in impairment of self-image, self-esteem, clinical depression, social phobia and anxiety [2]. Acne has multifactorial pathogenesis mainly follicular epidermal hyperproliferation, excess sebum production, inflammation and activity of *Propionibacterium acnes* [3].

Topical clindamycin and adapalene have additive effect not only for reducing comedones but also inflammatory acne lesions, reducing the duration of antibiotic therapy and the potential for developing bacterial resistance. Adapalene is an effective comedolytic [4].

Topical clindamycin and benzoyl peroxide has synergistic antimicrobial action. Clindamycin has anti-inflammatory action. Benzoyl Peroxide has keratolytic action and improves penetration of clindamycin [5]. Thus, the present

study was carried out to compare two different topical combination therapies in mild to moderate acne on face.

EXPERIMENTAL SECTION

A prospective, comparative efficacy and safety study was done after obtaining approval from institutional ethics committee and written informed consent from patients diagnosed with mild to moderate acne on face as per Indian Acne Alliance Grading for Severity of acne, aged between 12 to 25 years, of either sex, attending dermatology outpatient department at Victoria hospital, Bangalore, from november 2011 to may 2013. Patients not willing to give informed consent and follow up, those with other variants of acne, drug induced acne, pregnant and lactating mothers and those with history of hypersensitivity to any component of the drug were excluded from the study.

A randomization list was prepared by using table of random numbers and 120 patients diagnosed with mild to moderate acne on face were randomly assigned into 2 groups (A and B) of 60 each, Group A received combination of topical 1% clindamycin and 0.1% adapalene and Group B received combination of topical 1% clindamycin and 2.5% benzoyl peroxide.

For each patient, at baseline, details of sociodemographic data, history of acne, acne lesion counts and grade of acne was entered in the study proforma. Acne lesions were counted by the dermatologist and further these were noted as either noninflammatory or inflammatory acne lesions. Thus, total acne lesion count in each patient was considered as 100% at baseline. Baseline clinical grading of acne severity was done according to Indian Acne Alliance grading for severity of acne.

Treatment regimen was under the direction of treating dermatologist. Patients were advised to wash the face and dry it well before application.1 fingertip unit (approximately 0.5 gram) of each study drug was applied at bed time by dotting it over forehead, cheeks, chin and nose. A thin film was spread evenly over entire face avoiding periorbital, paranasal and perioral areas. Group A was advised to apply 0.1% adapalene gel and Group B 2.5% benzoyl peroxide gel first. After 5 minutes, both groups were advised to apply 1% clindamycin gel over it without washing the face and to leave the medication overnight. Initially if there was irritation with the drugs they were advised to begin with a short contact time of 15 – 30 minutes and then to gradually leave it overnight. If there was intolerable irritation initially, they were advised to wash it off and those patients will be excluded from the study.

Patients were followed up at the end of 4^{th} , 8^{th} and 12^{th} week for efficacy and safety evaluation. At each follow up compliance was assessed verbally.

Efficacy assessment was done by spot counting of acne lesions and comparing noninflammatory, inflammatory and total acne lesion counts at follow ups with their respective baseline lesion counts. If any reduction was noted, percentage reduction in acne lesion counts was calculated and expressed in terms of improvement in acne and graded.

Safety and tolerability was assessed by noting the local dryness , erythema , peeling, burning and irritation of skin and were further graded as mild, moderate and severe.

The data are expressed as mean, standard deviation for continuous measurements and number (%) for categorical measurements. To find the significance of study parameters on continuous scale between 2 groups student's T test (2 tailed, independent) was used and for the data on categorical scale Chi – square / Fisher exact test has been used. The level of significance was taken as $P \leq 0.05$ – significant, $P \leq 0.001$ – highly significant and $P > 0.05$ – not significant

RESULTS

The study enrolled 120 patients with 60 in each group. Out of 120 patients, 117 patients completed the study. 1 patient in group A and 2 patients in group B did not report for 4^{th} week and further follow up. Hence, they were excluded and for efficacy and safety assessment , 59 patients in group A and 58 patients in group B were included.
Both the treatment groups were comparable for their demographic characteristics and baseline disease characteristics with a similar mean number of noninflammatory, inflammatory and total acne lesions in each group [$P = 0.819$, 0.294 and 0.586 respectively] [Table – 1]

Table - 1: Demographic and baseline disease characteristics of patients in the 2 groups studied

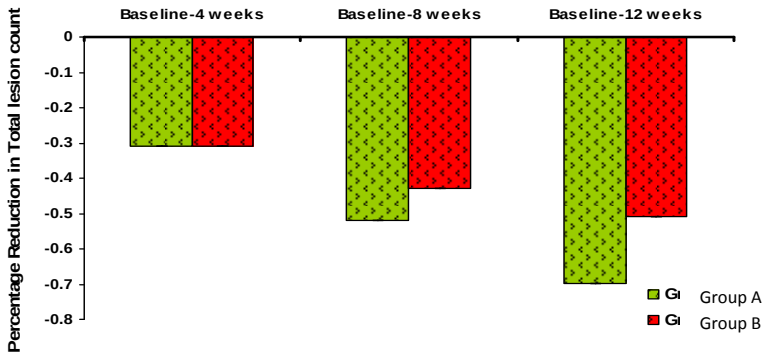
Characteristics	Group A (n = 60)	Group B (n = 60)	P value
Age (years)			
11 – 15	6 (10%)	0 (0%)	
16 – 20	49 (81.7%)	55 (91.6%)	
21 – 24	5 (8.3%)	4 (6.7%)	
>25	0 (0%)	1 (1.7%)	
Mean ± SD	17.85 ± 1.97	18.20 ± 1.73	0.310
Sex n (%)			
Male	35 (58.3%)	32 (53.3%)	
Female	25 (41.7%)	28 (46.7%)	0.581
Mean duration of acne (Years)			
< 1	6 (10%)	3 (5%)	
1 – 2	46 (76.7%)	49 (81.7%)	
>2	8 (13.3%)	8 (13.3%)	0.578
Baseline acne lesion counts			
Noninflammatory	37.35±10.43	36.9±11.11	0.819
Inflammatory	12.98±4.97	12.02±4.99	0.294
Total	50.33±13.33	48.97±14.08	0.586
Grade of acne			
Mild acne	18 (30%)	16 (26.7%)	
Moderate acne	42 (70%)	44 (73.3%)	0.685

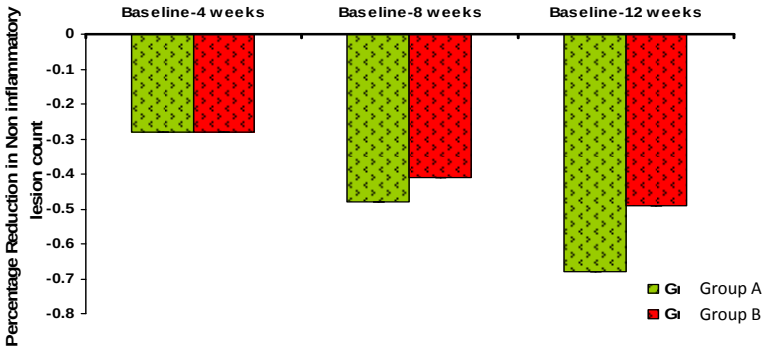
A*:Combination of topical 1% clindamycin and 0.1% adapalene gel,* ***B****: Combination of topical 1% clindamycin and 2.5% benzoyl peroxide gel,* ***SD****: Standard deviation*

Both treatment regimens reduced all types of acne lesion counts throughout the study period. [Figure 1]. Mean percentage reduction in total (-0.70±0.05 vs -0.51±0.03), noninflammatory (-0.68±0.07 vs -0.49±0.03) and inflammatory acne lesion counts (-0.77±0.06 vs -0.57±0.06) at 12 weeks was significantly greater in group A than group B (P < 0.001 for all types of acne lesion counts). [Table – 2]

Table – 2 : Comparison of mean percentage reduction in acne lesion counts at the end of 12 weeks in the 2 groups studied

Acne lesion counts	Group A (n = 59)	Group B (n = 58)	P value
Total acne lesions	-0.70±0.05	-0.51±0.03	<0.001**
Noninflammatory acne lesions	-0.68±0.07	-0.49±0.03	<0.001**
Inflammatory acne lesions	-0.77±0.06	-0.57±0.06	<0.001**





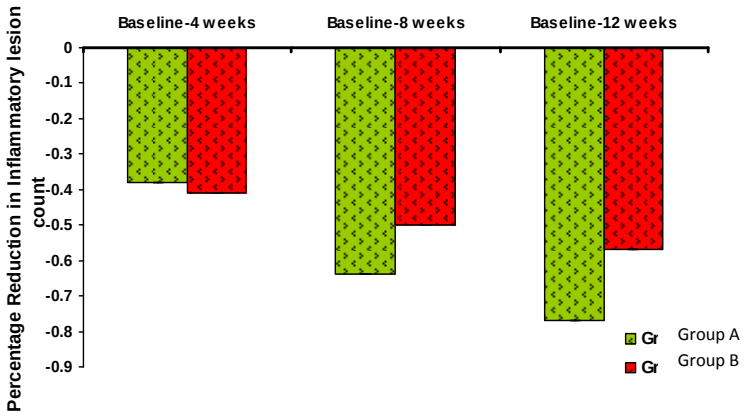


Figure – 1: **The mean percentage reductions in total, noninflammatory and inflammatory acne lesions during the course of the study as compared to baseline**

There was no significant differences between the groups in the number of patients reporting with local dryness (P = 0.434) and peeling of skin (P = 1.000). Erythema was significantly less in group A as compared to group B (P < 0.001). Similarly, the severity of local burning and irritation of skin was significantly less in group A as compared to group B (P < 0.027) [Table – 3]

Table – 3: Comparison of cumulative safety and tolerability parameters between the 2 groups studied

Cumulative Side effects	Group A (n=59)		Group B (n=58)		P value
	No	%	No	%	
Dryness					
No dryness	0	0.0	0	0.0	0.434
Mild dryness	22	37.3	17	29.3	
Moderate dryness	37	62.7	41	70.7	
Severe dryness	0	0.0	0	0.0	
Erythema					
No Erythema	58	98.3	13	22.4	<0.001**
Mild Erythema	1	1.7	27	46.6	
Moderate Erythema	0	0.0	18	31.0	
Severe Erythema	0	0.0	0	0.0	
Peeling					
No peeling	0	0.0	0	0.0	1.000
Mild peeling	27	45.8	26	44.8	
Moderate peeling	32	54.2	32	55.2	
Severe peeling	0	0.0	0	0.0	
Burning					
No burning	28	47.5	16	27.6	0.027*
Mild burning	31	52.5	42	72.4	
Moderate burning	0	0.0	0	0.0	
Severe burning	0	0.0	0	0.0	
Irritation					
No irritation	28	47.5	16	27.6	0.027*
Mild irritation	31	52.5	42	72.4	
Moderate irritation	0	0.0	0	0.0	
Severe irritation	0	0.0	0	0.0	

Table – 4: Comparison of grading of improvement in acne at the end of 12 weeks in the 2 groups studied

Grading of improvement in acne	Group A (n=59)		Group B (n=58)		P – value
	No	%	No	%	
Excellent (> 75% reduction in acne lesion count)	11	18.6	0	0.0	< 0.001**
Good (50 – 75% reduction in acne lesion count)	48	81.4	36	62.1	
Fair (25 – 50% reduction in acne lesion count)	0	0.0	22	37.9	
Poor (< 25% reduction in acne lesion count)	0	0	0	0	
Worse (Increase in acne lesion count)	0	0	0	0	

At the end of 12 weeks significantly more number of patients in group A showed an overall improvement in acne as compared to group B ($P < 0.001$) [Table – 4]

DISCUSSION

Topical combination therapy in acne aims at targeting different pathogenetic factors in acne. The results of the present study confirms the efficacy and safety of both combination therapies in mild to moderate acne. In our study, most acne patients were between 16 – 20 years of age (81.7 % and 91.6%) with a male preponderance (58.3% and 53.3%) in groups A and B respectively. Similar age distribution of acne (59.8%) was reported in a hospital – based study done in South India by B Adityan et al [6] with a male preponderance (55.7% vs 44.3%). Other previous studies done by JE Wolf et al [4], D Thiboutot et al [7], NB Reddy et al [8] reported a female preponderance while an equal male to female ratio was seen in the study done by VK Jain et al [9]. Thus, peak incidence in acne seen in adolescent age group may be due to various factors like peak increase in hormones in this age group [1] and also the psychosocial effects of acne [1] which may lead to increased tendency of patients to seek treatment. Male preponderance in our study reflects an increasing aesthetic concern in males similar to females.

The results of the previous studies,[4,8,10] with combination of topical 1% clindamycin and 0.1% adapalene in reducing total, noninflammatory and inflammatory acne lesion counts are as follows. JE Wolf et al [4] – 46.7%, 42.5% and 55.0%, NB Reddy et al [8] – 46.45%, 42.8% and 55.1% and S Prasad et al [10] – 62.7%, 58.4% and 71.4% for the conventional gel formulation while 79.7%, 74.9% and 88.7% for the nanoemulsion gel formulation while the results of our study with the above combination is (-0.70±0.05)% , (-0.68±0.07)% and (-0.77±0.06)% which is higher than the results of JE Wolf et al, NB Reddy et al and that seen with the conventional gel formulation in the study done by S Prasad et al but lesser than the nanoemulsion gel formulation of 1% clindamycin and 0.1% adapalene combination. Thus, variable treatment responses reported in the above studies emphasizes on the need for novel preparations of retinoid based combination therapies in acne for further significant increase in efficacy.

Similarly, the results of our study with the combination of topical 1% clindamycin and 2.5% benzoyl peroxide in the mean percentage reduction of total acne lesion counts (-0.51±0.03)% noninflammatory acne lesion counts (-0.49±0.03) %, inflammatory acne lesion counts (-0.57±0.06)% is similar to the study done by D Thiboutot et al [7] wherein, the mean percentage reduction in total acne lesion counts was (47.9%), for noninflammaory lesion counts (43.2%) and for inflammatory lesion counts (54.6%).

In terms of safety and tolerability profile of the combination of topical 1% clindamycin and 0.1% adapalene, in the Western study done by JE Wolf et al [4] reported that 25% of patients reported with erythema and 5% of the patients reported with stinging and burning sensation of moderate to severe intensity. In an Indian study done by S Prasad et al [10], moderate to severe erythema was seen in 9.9% of patients in the conventional group compared to 0.8% of patients in the nanoemulsion group. In our study, a very low incidence of erythema (1.7%) and mild irritation (52.5%) is reported. The difficulty in perception of erythema in Indian patients may be due to their generally darker skin complexion than the Caucasian patient population.

In terms of safety and tolerability profile of the combination of topical 1% clindamycin and 2.5% benzoyl peroxide, D Thiboutot et al [7] reported irritation in 0.1% of patients who also discontinued the study due to irritation. In our study, erythema and mild irritation was reported but there was no withdrawal from the study due to irritation. This may be due to the lower concentration of benzoyl peroxide which was better tolerated in our study.

CONCLUSION

Thus, greater and early treatment response with less irritation is noticed with the combination of topical 1% clindamycin and 0.1% adapalene treated group as compared to the combination of topical 1% clindamycin and 2.5% benzoyl peroxide treated group. Thus, the combination of topical 1% clindamycin and 0.1% adapalene is superior to the combination of topical 1% clindamycin and 2.5% benzoyl peroxide in the treatment of mild to moderate acne vulgaris.

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