Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Dermatology & Venereology

A Comparative Study to Evaluate the Efficacy and Safety of Clindamycin 1% with Adapalene 0.1% over Adapalene 0.1% alone in the Treatment of Mild to Moderate Facial Acne Vulgaris

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DOI: 10.36347/sjams.2023.v11i08.005 | **Received:** 28.05.2023 | **Accepted:** 20.06.2023 | **Published:** 08.08.2023

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Abstract **Original Research Article**

Background: Acne is an inflammatory disorder of pilosebaceous unit. Various topical medications are used for acne treatment such as antibiotics, retinoids, etc. Retinoids are commonly used to treat comedonal acne due to their keratolytic and anti-inflammatory properties. Antibiotics are effective against inflammatory acne lesions and are often combined with retinoids to minimize formation of antibiotic resistance. ***Objective:*** To compare safety and efficacy of clindamycin 1% with adapalene 0.1% combination over adapalene 0.1% alone in treatment of mild to moderate facial acne vulgaris. ***Methods:*** This interventional study was carried out in the department of Dermatology & Venereology of Enam Medical College and Hospital between January and December 2019. A total of 50 patients with mild to moderate facial acne who met the inclusion criteria and provided consent were enrolled in the study. They were divided into two groups as group A (clindamycin 1% with adapalene 0.1%) and group B (adapalene 0.1%) in a 1:1 ratio following a simple randomization method. Patients of both Group A and B were advised to apply topical adapalene gel 0.1% once daily for a period of 12 weeks. In addition, Group A patients were advised to apply topical clindamycin phosphate 1% lotion twice daily for 12 weeks. Patients were followed up on the 2nd, 4th, 8th and finally on 12th week to see clinical improvement and adverse effects. Clinical improvement was measured by reduction of acne lesions count between two groups. ***Results:*** Mean lesion count for open comedones, closed comedones, papules and pustules were identical between two groups at base line ($p>0.05$). Significantly better reduction of all type of acne lesions was observed during 2nd follow up onwards in group A compared to group B ($p<0.05$). Adverse effects were noticed significantly less in group A than in group B ($p<0.05$). ***Conclusion:*** Clindamycin phosphate 1% with adapalene 0.1% combination therapy was found to be safe and more effective than adapalene 0.1% monotherapy.

Keywords: Acne vulgaris, Clindamycin 1% lotion, Adapalene 0.1% gel.

INTRODUCTION

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous units, characterized by comedones, papules, pustules, nodules, pseudocysts and, in some cases, scarring [1]. It is the most common dermatological disease affecting approximately 85% of individuals aged between 12 and 24 years. Acne occurs due to hypercornification of the pilosebaceous unit, increased sebum production, colonization with propionibacterium acnes and inflammation [2]. While acne does not affect health overall, its impact on emotional well-being can be critical, often associated with depression and anxiety [3, 4].

Current treatments for acne include various topical and oral medications that counteract microcomedone formation, sebum production, P. acnes and inflammation. The topical compounds are benzoyl peroxide, antibiotics, and retinoids while tetracyclines, isotretinoin, cyproterone acetate and oral contraceptives are commonly used oral compounds [5]. Selection of topical therapy is based on acne type and severity. Topical retinoids, benzoyl peroxide, azelaic acid are effective for mild acne. Whereas topical antibiotics having bacteriostatic, and anti-inflammatory properties (e.g., clindamycin, erythromycin, etc.) are effective in mild to moderate acne [6].

Adapalene is a topical synthetic retinoid analogue derived from naphthoic acid. It inhibits the inflammatory response to bacterial antigens and decreases micro comedone formation [7, 8]. Adapalene has higher efficacy and tolerance than other concurrent acne medications, which makes topical adapalene a key component in the treatment of both comedonal and inflammatory acne [9].

Clindamycin is a lincosamide antibiotic with bacteriostatic effect. It inhibits bacterial protein synthesis blocking ribosomal translocation [10]. Topical clindamycin rarely causes skin irritation and even after 8 weeks of daily therapy, does not cause detectable levels of drug in urine. Clindamycin showed significant reduction in facial acne and has more efficacy than tetracycline, hence preferred over the later [11].

The preferred treatment for mild acne is topical medications containing antibiotics and/or retinoids. For moderate acne, systemic antimicrobials with topical retinoids are the choice [9]. It takes eight weeks for a microcomedone to mature. Thus, any therapy must be continued beyond this duration in order to assess efficacy [12]. Both adapalene and clindamycine have shown promises in the treatment of mild to moderate acne, however there is hardly any local data available to assess the comparative efficacy and safety trial on facial acne vulgaris with combination of topical clindamycin 1% and adapalene 0.1% vs adapalene 0.1% alone. Under these circumstances, this prospective study was carried out with an aim to find out the safety of topical clindamycin 1% with adapalene 0.1% in treatment of facial acne vulgaris and to determine the advantage of topical clindamycin 1% with adapalene 0.1% over adapalene 0.1% alone in the treatment of mild to moderate facial acne vulgaris and also to monitor the adverse effects encountered during therapy including follow-up treatment outcome.

MATERIALS AND METHODS

This prospective, open-labeled randomized, comparative interventional study was conducted on 50 patients with mild to moderate facial acne vulgaris who visited Dermatology and Venereology outpatient department of Enam Medical College and Hospital between the period of January 2019 to December 2019, a duration of 12 months. All patients who diagnosed as a case of mild to moderate facial acne vulgaris: comedonal, papular or pustular, patients of above 12 years of age and both sexes were enrolled in this study. Patients unwilling to give informed consent to take part in the study, pregnant and lactating women, females on oral contraceptives, patients with acne conglobata, acne fulminans, secondary acne, severe acne, patients with skin disease that may interfere with diagnosis/evaluation of acne vulgaris, other dermatologic conditions requiring systemic treatments, history of hypersensitivity to clindamycin and adapalene and use of any topical anti acne medications in past 14 days were excluded from the study.

All patients presented with acne were screened following the inclusion and exclusion criteria, then the first 50 patients who met those criteria and provided consent were enrolled in the study during study period at the study place. Informed written consent was at first obtained, then complete history taking, general, physical, and dermatological examinations was done for all enrolled patients. For women of reproductive age, reproductive history, menstrual history, lactation, and pregnancy was carefully judged. History and examination findings were recorded in a structured questionnaire.

At the time of enrolment, patients were randomized into two groups as group A (n= 25) and group B (n= 25) in a 1:1 ratio following a simple randomization method by allocating a random number for each patient. It was predetermined at the beginning of the study that patients getting even numbers would be placed in group A and those with odd numbers would be placed in Group B.

Group A received topical clindamycin phosphate 1% lotion twice daily in the morning and evening and adapalene gel 0.1% at night for a period of 12 weeks. Whereas Group B received topical adapalene gel 0.1% alone, once daily at night for a 12-week period. Patients were followed up on the 2nd, 4th, 8th and finally on 12th week to see clinical improvement and adverse effects. Patients were advised to wash their face with a suitable cleanser and dry it well. Adapalene gel was to be applied at night on entire susceptible areas with quantity such that it provides a thin layer covering the face.

- **Efficacy parameters:**

Number of non-inflammatory lesions (open and closed comedones), inflammatory lesions (papules and pustules), total lesions count was done on face at baseline and during treatment and at the end of 12 weeks. Clinical response was assessed by reduction of inflammatory, non-inflammatory and total acne lesions count between the groups. Percentage reduction of total acne lesions count was also performed.

- **Safety parameters:**

Each of the study participants were evaluated for symptoms and signs like erythema, scaling, itching, burning and dryness that indicates side effects of drugs on a scale from 0 (none), 1(mild), 2 (moderate) and 3 (severe) at each visit. Follow-up was done every 2, 4, 8 & 12 weeks and all the above parameters were evaluated at each visit. Tolerability scores were calculated at each visit by adding up the scores and

were compared. A lower score indicates fewer side effects.

All Data were collected at first using a structured paper-based questionnaire containing all the variables of interest. Data were then initially extracted in Microsoft Excel, coded, cleaned and then entered into Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA) for further statistical analyses. The mean values were calculated for continuous variables. Student t-test/unpaired t-test was used to compare continuous variables. The categorical variables were described by frequencies and percentages and then to compare Chi-Square test with Yates correction was used, shown with cross tabulation. All tests were performed at a 5% level of significance; thus, an association was significant(s) if the P value < 0.05 and non-significant (ns) if P value > 0.05.

RESULTS

There was a total of 50 patients, 25 patients in Group A and 25 patients in Group B. Group A. received topical clindamycin phosphate 1% lotion twice daily in the morning and evening and adapalene gel 0.1% at night for a period of 12 weeks. Group B. received topical adapalene gel 0.1% alone, once daily at night for a 12-week period.

Demographic Characteristics of the study participants

It was observed in our study that majority (44.0%) of the patients belonged to age 16-20 years in group A and 9 (36.0%) patients were of age ≤15 years in group B. The mean age was found to be 20.4±5.7 years in group A and 19.9±6.9 years in group B. The mean age difference was not statistically significant (p>0.05) between two groups.

Proportion of female was higher than male in group A, which was a 76.0% and 24.0% case respectively. Same is also true for group B, where proportion of female versus male was 84.0% vs 16.0% cases respectively. The difference between these two groups was not statistically significant (p=0.479).

Distribution of study participants on the basis of marital status showed that 18 (75.0%) of the patients were unmarried in group A and 20 (80.0%) in group B. The difference was not statistically significant (p>0.05) between two groups.

Occupational status of the study participants showed that, more than half (56.0%) of the patients were student in group A and 10 (40.0%) of the patients were housewife in group B. The difference was not statistically significant (p>0.05) between two groups.

In terms of socio-economic status of the study participants, it was observed that more than half (52.0%) of the patients came from middle class family in group A and 12 (48.0%) in group B. The difference was not statistically significant (p>0.05) between two groups (Table 1).

Table 1: Characteristics of the study participants

Characteristics	Group-A (n=25) n (%)	Group-B (n=25) n (%)	P value
Age			
≤15	05 (20.0)	09 (36.0)	0.781^{ns}
16-20	11 (44.0)	06 (24.0)	
21-25	05 (20.0)	04 (16.0)	
26-30	02 (08.0)	05 (20.0)	
>30	02 (08.0)	01 (04.0)	
Mean ± SD	20.4±5.7	19.9±6.9	
Sex			
Female	19 (76.0)	21 (84.0)	0.479^{ns}
Male	06 (24.0)	04 (16.0)	
Marital Status			
Married	18 (75.0)	20 (80.0)	0.674^{ns}
Single	07 (28.0)	05 (20.0)	
Occupation			
Service	04 (16.0)	03 (12.0)	0.661^{ns}
Housewife	07 (28.0)	10 (40.0)	
Student	14 (56.0)	12 (48.0)	
Socio-economic status			
Lower class	11 (44.0)	09 (36.0)	0.360^{ns}
Middle class	13 (52.0)	12 (48.0)	
Upper class	01 (04.0)	04 (16.0)	

ns = Not significant

Characteristics of the study participants based on age at onset and duration of disease

Mean age at onset was found 13.6±3.9 years in group A and 13.0±3.8 years in group B. Mean duration of disease was found 4.2±3.0 years in group A and 4.3±2.4 years in group B. The difference was not statistically significant (p>0.05) between two groups (Table 2).

Table 2: Distribution of the study patients by age at onset and duration of disease (n=50).

Characteristics	Group A (n=25)		Group B (n=25)		P-value
	Mean	±SD	Mean	±SD	
Age at onset (year)	13.6	±3.9	13.0	±3.8	0.584^{ns}
Duration of disease (in years)	4.2	±3.0	4.3	±2.4	0.907^{ns}

ns = Not significant

Comparison of Efficacy based on Acne lesions count between the groups before and after treatment

For open Comedones

At baseline before initiation of treatment there was no significant difference between the groups in regard to number of acne lesions. Even at the 1st follow-up no significant differences were observed. However, at successive follow ups different responses were observed between the two groups. At 2nd follow up, mean acne lesions count of open comedones was 2.15±0.36 in group A and 5.73±1.30 in group B. At 3rd follow up, mean acne lesions count of open comedones was found 1.88±0.28 in group A and 2.85±1.40 in group B. At 4th follow up, mean acne lesions count of open comedones was found 0.28±0.22 in group A and 2.20±1.13 in group B which was statistically significant (p<0.05) between two groups (Table 3 and Figure 1).

Table 3: Mean acne lesions count of open comedones in different follow up (n=50)

Open comedones	Group A (n=25)		Group B (n=25)		P value
	Mean	±SD	Mean	±SD	
Baseline	12.32	±1.25	12.46	±1.34	0.704^{ns}
1st follow up	9.84	±1.65	9.63	±1.27	0.616^{ns}
2nd follow up	2.15	±0.36	5.73	±1.30	0.001^{s}
3rd follow up	1.88	±0.28	2.85	±1.40	0.001^{s}
4th follow up	0.28	±0.22	2.20	±1.13	0.001^{s}

s= significant, ns = Not significant

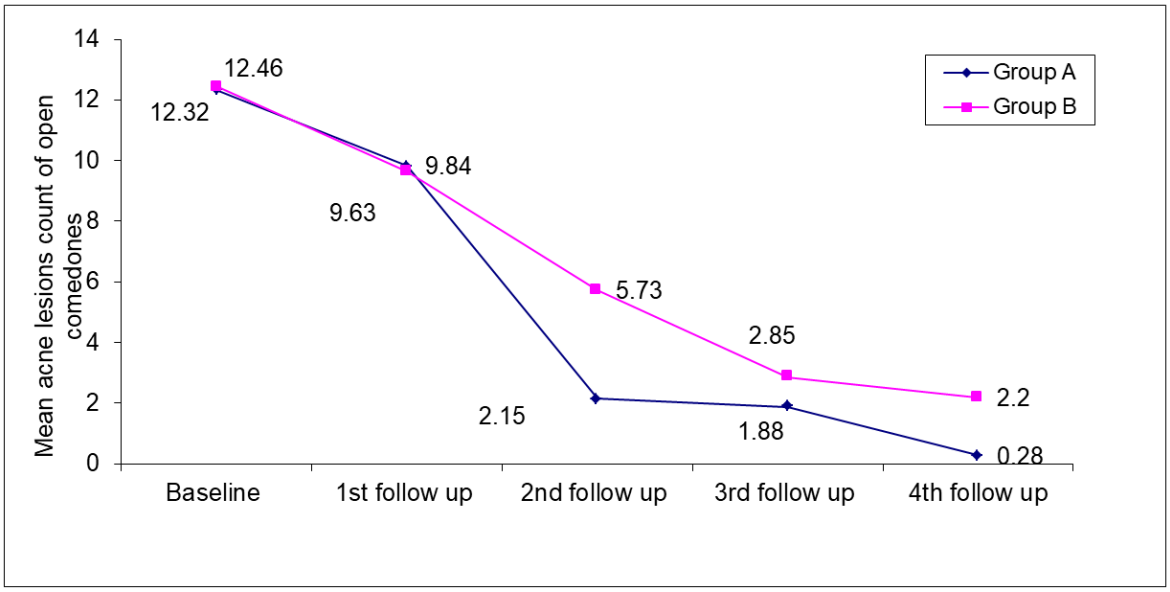

Figure 1: Line chart showing Mean acne lesions count of open Comedones in different follow up

For closed Comedons

At baseline before initiation of treatment there was no significant difference between the groups in regard to number of acne lesions. Even at the 1st follow-up no significant differences were observed. However, at successive follow ups different responses were observed between the two groups. At 2nd follow up, mean acne lesions count of closed comedones was found 5.91±1.06 in group A and 7.40±1.57 in group B. At 3rd follow up, mean acne lesions count of closed comedones was found 3.27±0.98 in group A and 4.03±1.07 in group B. At 4th follow up, mean acne lesions count of closed comedones was found 1.92±0.19 in group A and 2.08±0.25 in group B which was statistically significant ($p<0.05$) between two groups (Table 4 and Figure 2).

Table 4: Mean acne lesions count of closed comedones in different follow up (n=50)

Closed comedones	Group A (n=25)		Group B (n=25)		P value
	Mean	±SD	Mean	±SD	
Baseline	14.17	±2.43	14.21	±2.58	0.955^{ns}
1st follow up	10.44	±2.26	10.59	±2.37	0.819^{ns}
2nd follow up	5.91	±1.06	7.40	±1.57	0.001^{s}
3rd follow up	3.27	±0.98	4.03	±1.07	0.011^{s}
4th follow up	1.92	±0.19	2.08	±0.25	0.014^{s}

s= significant, ns = Not significant

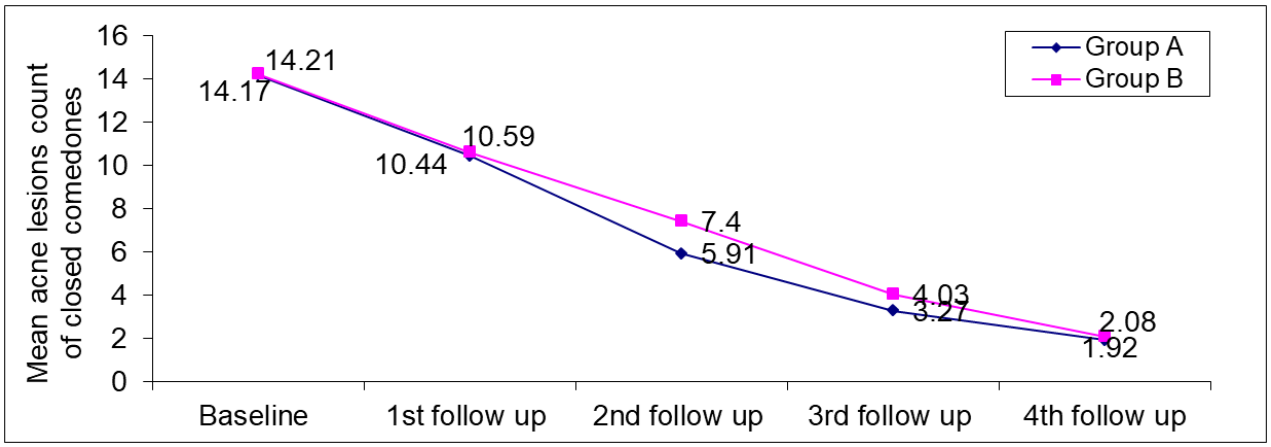

Figure 2: Line chart showing Mean acne lesions count of closed Comedones in different follow up

For Papules

At baseline before initiation of treatment there was no significant difference between the groups in regard to number of acne lesions. Even at the 1st follow-up no significant differences were observed. However, at successive follow ups different responses were observed between the two groups. At 2nd follow up, mean acne lesions count of papules was found 3.92±1.47 in group A and 4.94±1.63 in group B. At 3rd follow up, mean acne lesions count of papules was found 2.67±0.92 in group A and 3.80±1.12 in group B. At 4th follow up, mean acne lesions count of papules was found 0.82±0.29 in group A and 1.27±1.04 in group B which was statistically significant ($p<0.05$) between two groups (Table 5 and Figure 3).

Table 5: Mean acne lesions count of papules in different follow up (n=50)

Papules	Group A (n=25)		Group B (n=25)		P value
	Mean	±SD	Mean	±SD	
Baseline	9.60	±2.18	9.71	±2.61	0.872^{ns}
1st follow up	6.12	±1.69	6.80	±1.73	0.166^{ns}
2nd follow up	3.92	±1.47	4.94	±1.63	0.024^{s}
3rd follow up	2.67	±0.92	3.80	±1.12	0.001^{s}
4th follow up	0.82	±0.29	1.27	±1.04	0.042^{s}

s= significant, ns = Not significant

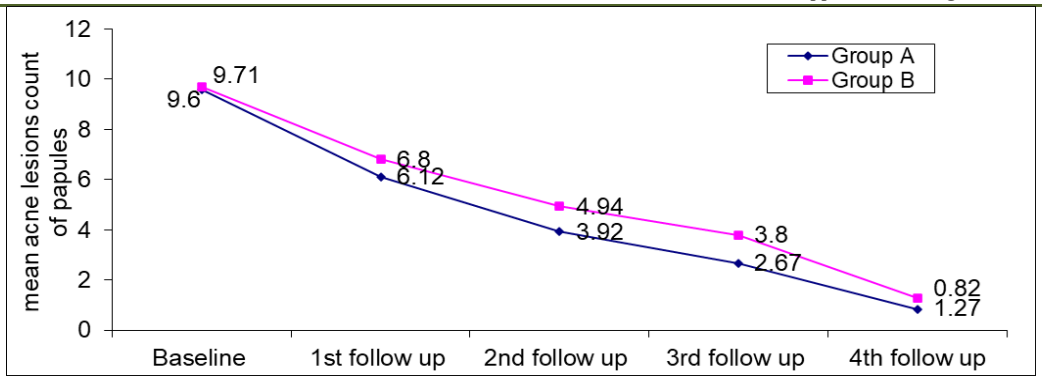

Figure 3: Line chart showing Mean acne lesions count of Papules in different follow up

For Pustules

At baseline before initiation of treatment there was no significant difference between the groups in regard to number of acne lesions. Even at the 1st follow-up no significant differences were observed. However, at successive follow ups different responses were observed between the two groups. At 2nd follow up, mean acne lesions count of pustules was found 2.09±1.09 in group A and 2.92±1.30 in group B. At 3rd follow up, mean acne lesions count of pustules was found 1.04±0.50 in group A and 1.83±1.05 in group B. At 4th follow up, mean acne lesions count of pustules was found 0.85±0.33 in group A and 1.19±0.39 in group B which was statistically significant ($p<0.05$) between two groups (Table 6 and Figure 4).

Table 6: Mean acne lesions count of pustules in different follow up (n=50)

Pustules	Group A (n=25)		Group B (n=25)		P value
	Mean	±SD	Mean	±SD	
Baseline	4.01	±2.44	4.45	±2.40	0.523[ns]
1st follow up	3.18	±1.88	3.54	±1.92	0.506[ns]
2nd follow up	2.09	±1.09	2.92	±1.30	0.018[s]
3rd follow up	1.04	±0.50	1.83	±1.05	0.001[s]
4th follow up	0.85	±0.33	1.19	±0.39	0.001[s]

s= significant, ns = Not significant

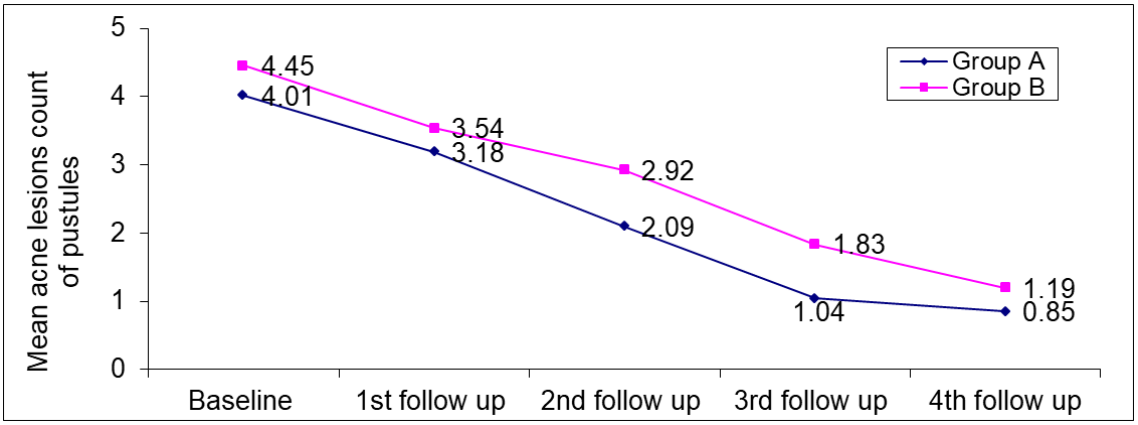

Figure 4: Line chart showing Mean acne lesions count of Pustules in different follow up

Total acne lesions count

At baseline before initiation of treatment there was no significant difference between the groups in regard to number of acne lesions. Even at the 1st follow-up no significant differences were observed. At 2nd follow up, mean of total acne lesions count was found 14.07±1.81 in group A and 20.99±1.86 in group B. At 3rd follow up, mean of total acne lesions count was found 8.86±0.97 in group A and 12.51±0.80 in group B. At 4th follow up, mean of total acne lesions count was found 3.87±0.69 in group A and 6.74±0.53 in group B. Percent reduction of total acne lesions from base line to final follow up, was 90.30±3.38 in group A and 83.50±3.51 in group B which was statistically significant ($p<0.05$) between two groups (Table 7 and Figure 5).

Table 7: Mean of total acne lesions count in different follow up (n=50)

Total acne lesions count	Group A (n=25)		Group B (n=25)		P value
	Mean	±SD	Mean	±SD	
Baseline	40.1	0±4.43	40.83	±4.26	0.555[ns]
1st follow up	29.58	±3.60	31.56	±3.41	0.051[ns]
2nd follow up	14.07	±1.81	20.99	±1.86	0.001[s]
3rd follow up	8.86	±0.97	12.51	±0.80	0.001[s]
4th follow up	3.87	±0.69	6.74	±0.53	0.001[s]
Percent of reduction from base line to 4th follow up	90.30	±3.38	83.50	±3.51	0.001[s]

s= significant, ns = Not significant

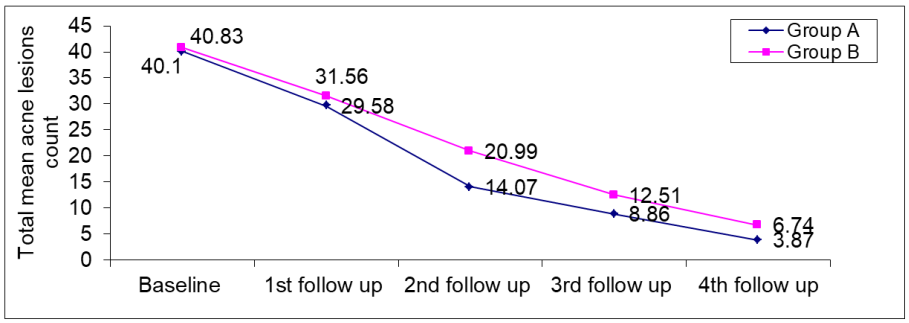

Figure 5: Line chart showing mean of total acne lesions count in different follow up

Comparison of adverse effects between the groups after treatment

At 4th follow up, mean erythema was found 0.67±0.55 in group A and 1.61±0.56 in group B. At 4th follow up, mean burning was found 0.15±0.08 in group A and 0.30±0.12 in group B. At 4th follow up, mean scaling was found 2.44±0.98 in group A and 3.05±0.98 in group B which were statistically significant (p<0.05) between two groups (Table 8).

Table 8: Tolerability score of erythema, burning, scaling, dryness and pruritus in 4th follow up (n=50)

Tolerability score	Group A (n=25)		Group B (n=25)		P value
	Mean	±SD	Mean	±SD	
Erythema	0.67	±0.55	1.61	±0.56	0.001[s]
Burning	0.15	±0.08	0.30	±0.12	0.001[s]
Scaling	2.44	±0.98	3.05	±0.98	0.032[s]
Dryness	0.86	±0.70	0.93	±0.74	0.732[ns]
Pruritus	0.51	±0.70	0.64	±0.66	0.502[ns]

s= significant, ns = Not significant

Total Tolerability score

At 1st follow up, the mean total tolerability score was found 12.16±1.09 in group A and 14.06±1.27 in group B. At 2nd follow up, the mean total tolerability score was found 8.78±0.87 in group A and 10.61±1.02 in group B. At 3rd follow up, the mean total tolerability score was found 5.04±1.05 in group A and 7.11±1.40 in group B. At 4th follow up, mean total tolerability score was found 3.05±0.92 in group A and 4.65±1.25 in group B which was statistically significant (p<0.05) between two groups (Table 9 and Figure 6).

Table 9: Total tolerability score in different follow up (n=50)

Total tolerability score	Group A (n=25)		Group B (n=25)		P value
	Mean	±SD	Mean	±SD	
1st follow up	12.16	±1.09	14.06	±1.27	0.001[s]
2nd follow up	8.78	±0.87	10.61	±1.02	0.001[s]
3rd follow up	5.04	±1.05	7.11	±1.40	0.001[s]
4th follow up	3.05	±0.92	4.65	±1.25	0.001[s]

s= significant

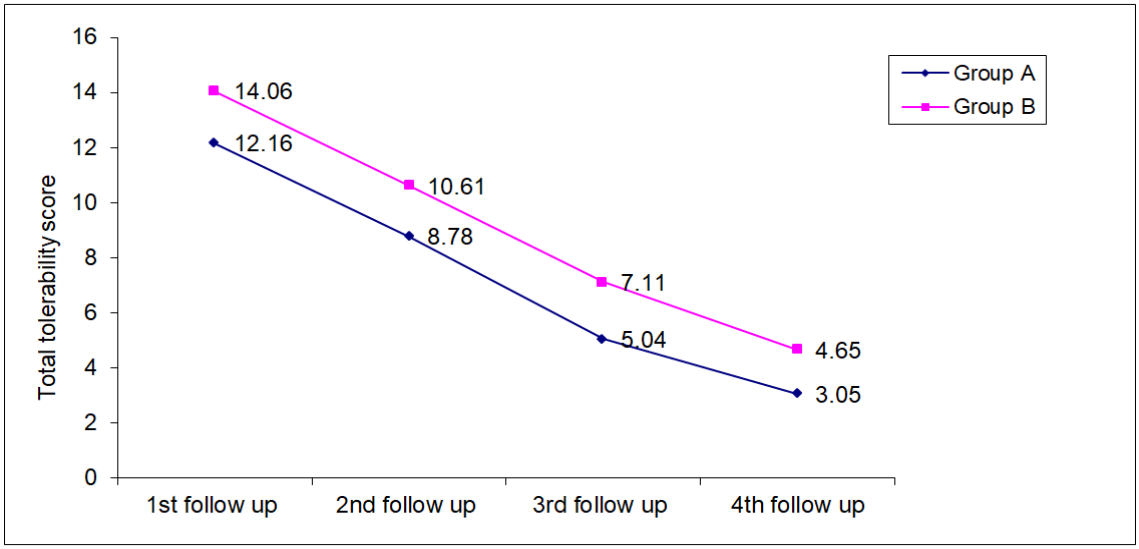

Figure 6: Line chart showing total tolerability score in different follow up

DISCUSSION

Acne vulgaris is a common skin disorder that is experienced by most people at some stage during their lifetime and accounts for approximately 25% of patient visits in private dermatology practice in the U.S.A. During the last 20 years, the number of topical and systemic drugs available for the treatment of acne vulgaris has increased, with many offers good efficacy. In a recent consensus conference, the combination of a topical retinoid and an antibiotic were recommended for the treatment of acne in a majority of patients [13]. Adapalene and clindamycin represent the groups respectively. Until now these two drugs were tested individually and found effective in treatment of acne. However, limited published evidence exists where their efficacy and safety has been evaluated when used in combination. Therefore, this prospective study was carried out with an aim to find out the safety of topical clindamycin 1% with adapalene 0.1% in treatment of facial acne vulgaris and to determine the advantage of topical clindamycin 1% with adapalene 0.1% over adapalene 0.1% alone in the treatment of mild to moderate facial acne vulgaris and also to monitor the adverse effects encountered during therapy including follow-up treatment outcome. In this present study, the mean age and standard deviation was 20.4±5.7 years in group A and 19.9±6.9 years in group B. It was observed that majority (44.0%) patients belonged to 16-20 years of age in group A whereas in group B, majority (36.0%) patients belonged to ≤15 years of age. Acne affects 95% of 16-year-old boys and 83% of 16-year-old girls to some degree. The incidence and severity of acne peaks at 14-17 years in girls and at 16-19 years in boys. Despite its spontaneous regression in most patients, acne persists in 10% of those patients over the age of 25 years [13]. Reddy and Nandimath found in their study that the peak prevalence age was 19.5 years. The number of cases reduced after 26 years of age [14].

It is often believed that there is no gender difference in acne prevalence, although such differences are often reported and, very likely, represent social biases [15]. In this current study it was observed that most of the patients were female in both group A and group B (76% vs 84% respectively). Male to female patients' ratio was almost 1:3 among the study participants. Reddy and Nandimath showed in a study of mild to moderate facial acne that 75.0% of the study participants were female [14]. Zhang *et al.,* [16] and Wolf *et al.,* [17] reported similar findings with female predominance in Acne related study. The above findings are consistent with the current study.

In this study, it was observed that the mean age of onset was found 13.6±3.90 years in group A and 13.0±3.80 years in group B. Similar findings were reported by Shen Y *et al.,* [18] and also by Li D *et al.,* [19].

In this study, at 2nd follow up, mean acne lesions count of open comedones was found 2.15±0.36 in group A and 5.73±1.30 in group B. At 3rd follow up, mean acne lesions count of open comedones was found 1.88±0.28 in group A and 2.85±1.40 in group B. At 4th follow up, mean acne lesions count of open comedones was found 0.28±0.22 in group A and 2.20±1.13 in group B which was statistically significant ($p<0.05$) between two groups.

At 2nd follow up, mean acne lesions count of closed comedones was found 5.91±1.06 in group A and 7.40±1.57 in group B. At 3rd follow up, mean acne

lesions count of closed comedones was found 3.27±0.98 in group A and 4.03±1.07 in group B. At 4th follow up, mean acne lesions count of closed comedones was found 1.92±0.19 in group A and 2.08±0.25 in group B which was statistically significant ($p<0.05$) between two groups.

At 2nd follow up, mean acne lesions count of papules was found 3.92±1.47 in group A and 4.94±1.63 in group B. At 3rd follow up, mean acne lesions count of papules was found 2.67±0.92 in group A and 3.80±1.12 in group B. At 4th follow up, mean acne lesions count of papules was found 0.82±0.29 in group A and 1.27±1.04 in group B which was statistically significant ($p<0.05$) between two groups.

At 2nd follow up, mean acne lesions count of pustules was found 2.09±1.09 in group A and 2.92±1.30 in group B. At 3rd follow up, mean acne lesions count of pustules was found 1.04±0.50 in group A and 1.83±1.05 in group B. At 4th follow up, mean acne lesions count of pustules was found 0.85±0.33 in group A and 1.19±0.39 in group B which was statistically significant ($p<0.05$) between two groups. Mean lesions count for open comedones, closed comedones, papules and pustules were identical between two groups at base line ($p>0.05$). Significantly better reduction of open comedones, closed comedones, papules, pustules individually and total acne lesions count was noticed at 2nd and 3rd follow up ($p<0.005$) in group A than in group B.

At 2nd follow up, mean of total acne lesions count was found 14.07±1.81 in group A and 20.99±1.86 in group B. At 3rd follow up, mean of total acne lesions count was found 8.86±0.97 in group A and 12.51±0.80 in group B. At 4th follow up, mean of total acne lesions count was found 3.87±0.69 in group A and 6.74±0.53 in group B. Percent reduction of acne severity from base line to final follow up was 90.30±3.38 in group A and 83.50 ± 3.51 in group B. Percent reduction of acne severity was significantly higher ($P<0.05$) in group A.

Reddy and Nandimath showed in a study that there were significantly greater reductions in inflammatory, non- inflammatory and total acne lesions in adapalene plus clindamycin group than in adapalene 0.1% treated group. The combination of adapalene and clindamycin significantly reduced the number of both inflammatory and non-inflammatory acne lesions, with an approximately 25% greater reduction in inflammatory acne lesions (55.0% vs. 44.2%) and a 2-to-3- fold greater reduction in non-inflammatory acne lesions (42.5% vs. 16.3%) than adapalene group at week 12. Patients also demonstrated a faster response to the combination therapy, with a statistically significantly greater improvement in the reduction of total inflammatory and non-inflammatory acne lesions seen as early as week 4. The significantly greater and faster effect on acne lesions obtained by adding adapalene to clindamycin indicates that this combination can be used at the onset of therapy to obtain a better clinical response than that obtained by the use of adapalene alone. Adapalene has a significant anti-inflammatory effect that enhances the therapeutic action of clindamycin on inflammatory acne lesions [14]. Wolf Jr *et al.*, and Kubota Y *et al.*, also reported significant improvement in all forms of acne among the group treated with clindamycin and adapalene [17,20]. The above study findings are similar to the present study.

According to tolerability score at 4th follow up, mean erythema was found 0.67±0.55 in group A and 1.61±0.56 in group B. At 4th follow up, mean burning was found 0.15±0.08 in group A and 0.30±0.12 in group B. At 4th follow up, mean scaling was found 2.44±0.98 in group A and 3.05±0.98 in group B which was statistically significant ($p<0.05$) between two groups. However, dryness and pruritus were less observed in group A than group B but the difference was not statistically significant ($p<0.05$). Wolf *et al.*, analyzed the severity of erythema, scaling, dryness, and stinging/burning and their results showed that scaling, dryness, and stinging/burning were greater in the clindamycin plus adapalene group when compared to clindamycin alone group. Though in most cases these symptoms were mild in intensity [17].

At 1st follow up, the mean total tolerability score was found 12.16±1.09 in group A and 14.06±1.27 in group B. At 2nd follow up, mean total tolerability score was found 8.78±0.87 in group A and 10.61±1.02 in group B. At 3rd follow up, the mean total tolerability score was found 5.04±1.05 in group A and 7.11±1.40 in group B. At 4th follow up, mean total tolerability score was found 3.05±0.92 in group A and 4.65±1.25 in group B. Events of adverse effects as indicated by total tolerability score was significantly less in group A than group B ($p<0.0501$).

CONCLUSION

In conclusion, results of our present study revealed that, the combination regimen of clindamycin 1% plus adapalene 0.1% is indeed very much efficacious and safe than adapalene 0.1% alone.

Strength and Limitations of the study

Although this study was important due to its unique nature of being the first study done in low-resource setting exploring the efficacy of the combination regimen of clindamycin 1% plus adapalene 0.1% compared to adapalene 0.1% alone in treatment of acne vulgaris, nonetheless, these results must be interpreted with caution and a number of limitations should be borne in mind. The first limitation was that

the study population, which was selected from one selected hospital of Dhaka city, so that the results of the study might not reflect the exact picture of the whole country.

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