Comparative study on efficacy of benzoyl peroxide with adapalene versus plain adapalene in the treatment of acne vulgaris

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ABSTRACT

BACKGROUND

Acne vulgaris is a dermatological disorder of pilosebaceous unit, characterized by formation of comedones and inflammatory lesions. It is one of the most common skin manifestations among adolescents, also affecting the adult population. The treatment of acne basically involves reduction of lesions and prevention of permanent scarring. The current line of treatment for mild to moderate acne is topical medications with antimicrobials and retinoids. The present study assessed the efficacy of combination of adapalene and benzoyl peroxide in comparison to adapalene for topical treatment of mild to moderate acne vulgaris.

OBJECTIVE

The purpose of the study was to compare the clinical efficacy of topical adapalene and topical adapalene with benzoyl peroxide in treatment of mild to moderate cases of acne vulgaris.

METHODOLOGY

A prospective, comparative study was carried out among 84 patients with mild and moderate acne vulgaris visiting the Department of Dermatology, Kathmandu Medical College and Teaching Hospital, Bhaktapur, Nepal from December 2019 till March 2021. The patients fulfilling the inclusion criteria were divided into two groups. Group A received topical adapalene whereas Group B received topical adapalene with benzoyl peroxide. The efficacy of treatment in both groups were determined based on the reduction of total lesion count. Both inflammatory and non-inflammatory lesions were counted at 4th week, 8th week and 12th week.

RESULTS

All patients were assessed according to Global Acne Grading System (GAGS) and grouped as mild and moderate. The most frequent age group affected by acne vulgaris was 18-22 years. The mean age was 22.15 ± 5.315. Females (64.30%) were affected more commonly than males (35.7%). Majority of patients presented with moderate or inflammatory acne lesions. The face (90.5%) was most commonly affected site by acne vulgaris. The number of patients enrolled in the study were 84 out of which 63 (75%) completed the study. It was found that the reduction of non-inflammatory, inflammatory and total lesion count from the baseline were highly significant in between and both the group (P<0.001). A total of 52.4% had very good result of the treatment, 44.4% of them had good result and remaining 3.2% of the patients' result was fair. However, the efficacy of benzoyl peroxide with adapalene was found to be better than adapalene alone.

CONCLUSIONS

This study concluded that topical benzoyl peroxide with adapalene is more efficacious to treat mild to moderate acne vulgaris.

KEY WORDS

Acne vulgaris, topical, adapalene, benzoyl peroxide with adapalene, efficacy

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BACKGROUND

Acne vulgaris is one of the most common skin disorders. It affects up to 80% of adolescents. Although it usually manifests during puberty and worsens throughout adolescence, epidemiological studies suggest that it can arise at any age; from childhood to adulthood.[1,2] Acne vulgaris is seen to persists beyond the age of 25 years in 3% of men and 12% of women.[3] Acne may cause significant psychological and social problems, depression, low self-esteem, disfigurement and scarring that can persist for a lifetime. Also it can cause occupational consequences to potential psychiatric disturbances such as depression.[4]

Acne vulgaris is a chronic disease due to its long duration and recurring nature. Inflammatory or non-inflammatory lesions and varying degrees of scarring characterize Acne vulgaris.[5] The main etiologies involved are hormonal, genetic, psychological, infectious and diet.[6]

It has various clinical presentations characterized by seborrhea, erythematous papules and pustules, comedones, nodules or pseudocysts.[1] The areas affected are face, cheeks, nose, forehead, chest, back and arms.[7]

Acne severity is classified according to different scales. Mild to moderate forms are mostly considered primary acne lesions while severe acne includes nodules, cysts, and eventually open lesions. This mild form of acne, sometimes called "physiologic acne" with relatively few "pimples" and "blackheads", accounts for 60% of the cases and responds well to over-the-counter products. Around 40% of patients with more severe "clinical acne" require medical treatment.[8, 9]

Acne affects the face in a majority of cases; mainly cheeks, nose, forehead and also the chest, back and arms.[1, 7] Many patients experience some degree of scarring after acne resolution which can be emotionally and psychologically distressing. Studies report the incidence of acne scarring in the general population to be 1 to 11%. The severity of scarring correlates to acne grade. Almost all scars (99%) originate from papules and pustules (inflammatory lesions) and post-inflammatory lesions.[10]

There are different treatment modalities for acne vulagris.[1] Antibiotics targeting P. acnes have been the mainstay in acne treatment for the past four decades. Among them, macrolides, clindamycin, and tetracyclines are the most widely prescribed.

Topical treatment is the mainstay of acne therapy. Benzoyl peroxide is the most commonly used and has been an important component of topical therapy for acne vulgaris for more than five decades. It markedly reduces P. acne thereby preventing the formation of comedones caused by the same. It is effective for the treatment of mild to moderate lesions.[1,24] Topical BP also has mild sebostatic effects contributing to its keratolytic activity and efficacy in treating comedonal acne.[6] It decomposes to release free oxygen radicals which are potent bactericidal. It reduces follicular hypertrophies and has anti-inflammatory properties.[2] It is also shown to reduce the number of antibiotic resistant organisms.[1] BP is available as both over-the-counter and prescription formulations in concentrations of 2.5%, 5%, and 10%.[25] Available preparations include lotions, creams, gels, foams, solutions, cleansing bars, cleansing lotions, cloths, pads, masks, and shaving creams. Benzoyl peroxide is often combined with topical antibiotics. Adapalene is a topical retinoid compound capable of binding to specific retinoic-acid nuclear receptors. It is a naphthoic acid derivative and available in various forms like gel, cream and solution.[27] It has anti-inflammatory and keratolytic action within pilosebaceous duct.[1,2,5] The combination has been shown to give a faster response than the benzoyl peroxide alone.[1]

Acne vulgaris is associated with symptomatic discomfort and emotional distress. It is a common condition with wide range of potential harms such as occupational consequences and psychiatric disturbances including depression. It can result in physical scarring if left untreated. Also its treatment is associated with a wide range of cost. Benzoyl peroxide with adapalene is one of the most effective and widely used drugs, is available in many over-the-counter preparations and is able to reduce both non-inflammatory and inflammatory lesions.

The study was conducted to compare the efficacy of benzoyl peroxide with adapalene versus plain adapalene for treatment of acne vulgaris in Kathmandu Medical College and Teaching Hospital, and to find the efficacy of topical benzoyl peroxide with adapalene in patients of acne vulgaris (Grade 1 and 2).

METHODOLOGY

Sample collection and scoring

This research was a prospective comparative study carried out in the Department of Dermatology, KMCTH. Diagnosed cases of Grade 1 and Grade 2 acne vulgaris between the age of 13-40 years reporting in the OPD of Dermatology Department were included in the study. Ethical clearance was taken from Institutional Review Committee of KMCTH. Permission was given by the Head of Department (HOD) of Dermatology, KMCTH. All the participants were informed about the study and written consent was taken. Participants were explained about the study, procedure and its significance in Nepali language before obtaining the consent. The patients included in this study were assured of full confidentiality during and after the study period and they voluntarily participated in the study.

The ethical approval for study was taken from Institutional Review Committee, Kathmandu Medical College and

Teaching Hospital, Duwakot, Bhaktapur before sample collection.

Convenient sampling method was opted. A total of 84 patients were recruited in the study (p= prevalence of acne = 10.1%12). Independent variables; Age and sex and dependent variables: non-inflammatory lesion count, Inflammatory lesion count, and Total lesion count were accessed in the study.

Patients with history of hypersensitivity to adapalene and benzoyl peroxide were excluded from the study. Also, pregnant and lactating mothers, patients taking or using any anti-acne drugs in prior weeks and those not willing to participate in the study were excluded. Patient's information and history were taken by using proforma enquiring about their name, age, address, drug prescribed, and the presence of inflammatory, non-inflammatory lesions.

Acne vulgaris was graded by Simple Grading System (SGS)[14]

  Grade 1: Comedones, occasionally papules

  Grade 2: Papules, comedones, few pustules

  Grade 3: Predominant pustules, nodules, abscesses

  Grade 4: Mainly cysts, abscesses, widespread scarring

Global Acne Grading System was used for determining the grade of acne and to assess the sites of involvement.

Global Acne Grading System (GAGS)14, 15

Location	Factor
Forehead	2
Right cheek	2
Left cheek	2
Nose	1
Chin	1
Chest and upper back	3

Note: 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 of each area (local area) is calculated using the formula: local score = Factor × Grade (0-4). The global score is the sum of local scores, and acne severity was graded using the global score. A score of 1-18 is considered mild; 19-30 moderate; 31-38 severe; and >39 very severe.

Grading	Score
Mild	1-18
Moderate	19-30
Severe	31-38
Very Severe	>39

The patients were divided into two groups Group A and Group B. Even number patient was included in Group A and odd number patient was included in Group B. Group A was treated with topical adapalene 0.1% gel and Group B was treated with benzoyl peroxide 2.5% with adapalene 0.1% gel.

The patients were advised to apply the gel once a day at night. They were advised not to use any other medicament during a period of 12 weeks.

Each patient was assessed at 4th week, 8th week and 12th week.

The efficacy assessment of the patients was done by lesion counting technique. The change of total lesion, both inflammatory and non-inflammatory lesions, count from baseline was the main efficacy parameter.

Grading of improvement in acne	
Excellent	>75% reduction in acne lesion count
Good	50-75% reduction in acne lesion count
Fair	25-50% reduction in acne lesion count
Poor	<25% reduction in acne lesion count
Worse	Increase in acne lesion count

RESULTS

The present study was conducted among 84 patients with acne vulgaris attending the OPD in Kathmandu Medical college and teaching hospital. The age of the patients who participated in the study ranged from 13 to 40 years. Majority of patients 34.5% belonged to age 18-22 years as shown in Fig.1. The mean age of the patients under study was 22.15 ± 5.315 (Mean ± SD).

(Minimum age = 14 years, Maximum age = 37 years, Median age = 21 years)

Majority of the patients were female (64.30%) (Fig. 2). A total of 58 (69%) patients presented with moderate acne vulgaris and 26(31%) patients presented with mild acne (Fig. 3). The most commonly involved site was face (90.5%) followed by acne at chest and/or back (29.8%). A total of 90% of acne was found to be present in the forehead, 82% in right cheek, 77% in left cheek, 54.80% lesions was seen in the right cheek and 48.8% was found on chin (Fig. 4, Fig. 5). Majority of patients belonged to the age category of 23-27 years in Group A, and to 18-22 years age category in Group B. Table 1 illustrates result of age wise distribution of patient in different drug groups. In group A, 28 (66.7%) were female and 14 (33.3%) were male. Whereas in group B, 26 (61.9%) were females and 16 (38.1%) were male. The results of gender wise distribution of patients in two drug groups are summarized in Table 2.

A total of 84 patients were enrolled in this study and out of which 63 (75%) completed. In group A 33 and groups B 30 completed the 12 weeks treatment. Table 3 illustrates clinical evaluable patients in both drug groups. A total of 52.4% patients had very good result (>75% reduction), 44.4% of them

had good results (50-75% reduction) and 3.2% had fair results (<25% reduction) at the end of 12 weeks therapy. The result obtained is summarized in Table 4. There was statistically significant percentage reduction of non-inflammatory lesions, inflammatory and total lesions at each visit in both the groups as well as between Group A and Group B (p< 0.001). This is illustrated in Table 5.

There was reduction in the number of both non-inflammatory lesions, inflammatory lesions and total number of lesions at the end 12 weeks of therapy in both groups. This is illustrated in Table 6. There was statistically significant reduction in the mean scores of non-inflammatory lesions, inflammatory and total lesions at each visit in both the groups as well as between Group A and Group B (p< 0.001). This is illustrated in Table 7.
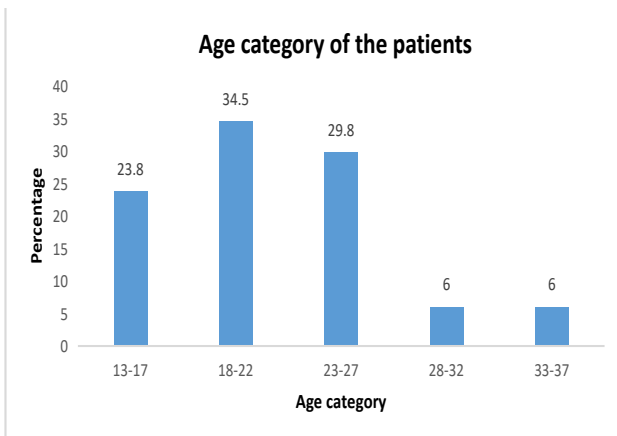

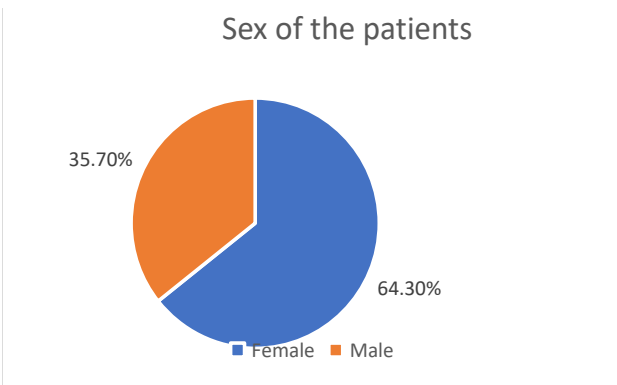Fig. 1. Age wise distribution of patients with acne vulgaris

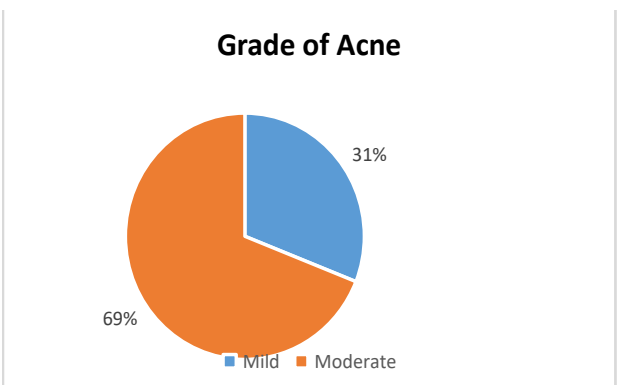Fig. 2. Gender distribution of patients with acne vulgaris

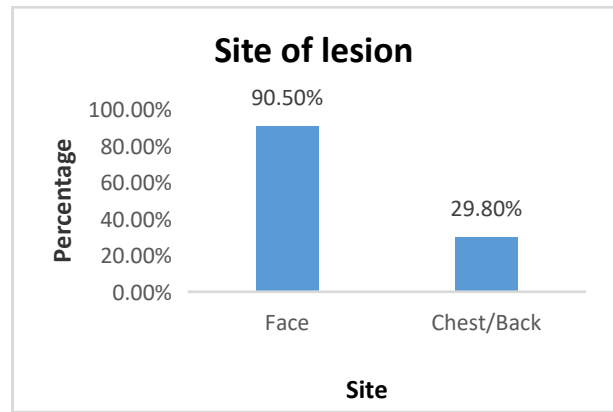Fig. 3. Distribution of Grade 1 and Grade 2 lesions of acne vulgaris

Fig. 4. Distribution of acne vulgaris at different sites

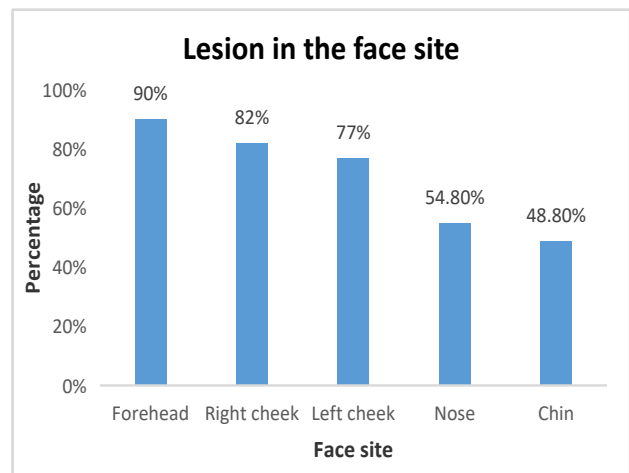Fig 5. Distribution of acne in face

Table 1: Age wise distribution of patient in different drug group

Age category	Treatment Category		Total
	Group A	**Group B**	
13-17 years	9	11	20
18-22 years	11	18	29
23-27years	15	10	25
28-32years	4	1	5
33-37 years	3	2	5
Total	**42**	**42**	**84**

Table 2: Gender distribution of patients in different drug groups

Gender	Group A		Group B		Total	
	N	%	N	%	N	%
Male	14	33.3	16	38.1	30	35.7
Female	28	66.7	26	61.9	54	64.3

Table 3: Clinical evaluable patients in two drug groups

N (42)		Group A (Adapalene)		Group B (A/ BPO)	
		100 %	N (42)	100 %	
4 weeks	Clinical evaluable	41	97.6%	39	92.8%
	Lost to follow up	1	2.4%	3	7.2%
8 weeks	Clinical evaluable	39	92.8%	36	85.71%
	Lost to follow up	3	7.2%	6	14.29%
12 weeks	Clinical evaluable	33	78.57%	30	71.42%
	Lost to follow up	9	21.43%	12	28.58%
Total		**33**	**52.3%**	**30**	**47.6%**

Table 4: Grading improvement of Acne vulgaris at the end of 12 weeks

Grading of improvement of acne	Group A		Group B		Total		P-value
	N	%	N	%	N	%	
Very good	5	15.2	28	93	33	52.4	
Good	26	78.8	2	6.7	28	44.4	
Fair	2	6.1	0	0	2	3.2	<0.001
Total	33	100	30	100	63	100	

Table 5: Comparison of percentage reduction of non-inflammatory, inflammatory and total lesion

Parameters	Drugs	4th week	8th week	12th week	P-value
NIL	Group A	18.2	41.6	66.5	
	Group B	29.8	57.8	78.1	
IL	Group A	26.3	49.3	67.6	P<0.001
	Group B	42.2	69.6	87.4	
TLC	Group A	22.1	45.2	67	
	Group B	34.5	62.9	81.7	

NIL- Non-inflammatory lesions; IL- Inflammatory lesion

TLC- Total lesion count

Table 6: Comparison of lesions before and after treatment

Parameters	Drugs	Baseline	After12 week
Non-inflammatory lesion	Group A	369	127
	Group B	354	81
Inflammatory lesion	Group A	291	95
	Group B	258	34
Total lesion	Group A	660	222
	Group B	612	115

Table 7: Comparison of mean score of lesions at each visit

Parameters	Drug Groups	1st day	4 weeks	8 weeks	12 weeks	P-value
NIL	Group A	11.2±4.1	9±3.2	6.4±2.4	3.9±2	<0.001
	Group B	11.3±4.1	8.1±3.2	4.9±2.3	2.7±1.5	<0.001
IL	Group A	9.0±1.7	6.6±1.3	4.5±1.1	2.9±1.2	<0.001
	Group B	8.8±2	5.1±1.4	2.7±1	1.1±0.8	<0.001
TLC	Group A	20±4.7	15.4±3.8	10.9±2.9	6.7±2.7	<0.001
	Group B	20.1±4.2	13.3±3.3	7.6±2.5	3.8±1.6	<0.001

DISCUSSION

Acne vulgaris is one of the most commonly encountered dermatological problems worldwide in both primary and secondary care.16 It is an almost universal disease with worldwide prevalence of 9.4%.17 The clinical presentation can vary from mild non-inflammatory lesions to severe, and can lead to permanent hyperpigmentation and scarring.9 Acne vulgaris results from the inflammation of pilosebaceous unit of the skin. Blockage of sebaceous glands and colonization with Propionibacterium acnes leads to acne.1,3 Although acne does not cause any serious health effects, it may lead to significant social and psychological problems, low self-esteem and depression.4

In the present prospective study conducted in Department of Dermatology at Kathmandu Medical College and teaching Hospital, Bhaktapur, Nepal from December 2019 to March 2021, 84 patients of acne vulgaris were enrolled. Equal number patients were divided into two groups, one group was treated with adapalene while another was treated with the combination of benzoyl peroxide with adapalene. The main objective of the study was to compare the efficacy of these drugs in diagnosed cases of Grade 1 and Grade 2 acne vulgaris. In total 84 patients enrolled in the study out of which 63 (75%) completed the 12 weeks treatment.

In this study the incidence of acne vulgaris was higher in the age group 18-22 (34.5%). The mean age of the patients was 22.15 ± 5.315 years In the result of the study done by the most common age group is 11-20 and the mean age of the patient was 22.1+_6.5.(88) Similarly a study conducted in Nepal among 100 school students showed most of the students with acne belonged to age group of 15-17 years.18 According to the Global Burden of Disease (GBD) study, acne vulgaris affects approximately 85% of young adults aged 12−25 years.19 The production of androgens during puberty explains, in part, why acne vulgaris is so prevalent in this population. The production of androgens is high during puberty and thus enhanced sebaceous acitivity.19 During and around puberty onset, androgens are in high levels. The primary androgen DHEA-S is responsible for sebum production. Weak DHEA-S is converted into potent androgens by enzymes present in sebocytes. These are responsible for increased proliferation of sebaceous glands and increased sebum production.20

The prevalence of acne vulgaris was found to be 64.3% in females and 35.7% in males (with female to male female ratio of 1.8:1). It is similar to the findings by Yang et al21 in Taiwan. Similarly, the disease was more common among females in studies done by Noorbala et al22 in Iran, Tayel et al23 in Egypt, Jusuf et al24 in Indonesia, and Zohra et al7 in Bangladesh. An earlier puberty onset for females triggers a higher incidence of acne vulgaris throughout all ages compared to men. The factors attributing to the incidence difference seen between males and females are likely complex and multifactorial. The higher incidence of acne among women may be due to greater attention to skin care, the use of certain cosmetics, hormonal imbalance, or diet.4, 19, 25

A total of 59% of patients presented with moderate or inflammatory acne lesions and remaining 31% had mild acne lesions. Inflammatory acne was the predominant type observed in both males and females in a study of 200 diagnosed cases of acne vulgaris conducted by Al-Ameer et al 26 in Saudi Arabia. The findings of this study are also in line with those noted by Goulden et al.27

In this study, the most commonly involved site was face (90.5%) followed by acne at chest and/or back (29.8%), which confirms to the observation by Cunliffe et al 28 and Tan J et al.4 Pandey et al29 found that maximum number 63.7% of patients presented

with lesions over face followed by 14.7% of patients having lesions over face and back in a cross-sectional study in India. Acne affects the facial region in a majority of cases.3,7 The largest and greatest number of sebaceous glands are found on the face, upper trunk and scalp.20 The sebaceous gland is an important site for androgen processing and modulation. All of the enzymes necessary for transforming cholesterol to steroids or adrenal precursors, such as dehydroepiandrosterone, are found in the sebaceous glands of skin.29

Overall, a total of 52.4% patients had more than 75% of reduction in total number of lesion, 44.4% of them had good results and 3.2% of them had fair reduction of acne at the end of 12 weeks (p< 0.001). Sittart et al30 concluded that overall, majority of patients had an improvement varying from good to excellent and only few had fair results.

In Group A, the mean score of non-inflammatory lesions was 11.2 at the first visit (baseline), which was reduced to 9, 6.4 and 3.9 at the end of 4, 8 and 12 weeks respectively. The mean score of inflammatory lesions was 9 at the first visit, which was reduced to 6.6, 4.5 and 2.9 at the end of 4, 8 and 12 weeks respectively. Whereas the mean score of total lesions was 20 during the first visit, which was reduced to 15.4, 10.9 and 6.7 at the end of 4, 8 and 12 weeks respectively. The reduction seen were statistically significant at each visit (p < 0.001) for both inflammatory, non-inflammatory lesions and total lesions. Confirming to this, the reduction in inflammatory lesion and total lesion was statistically significant (p <0.05) when Diba et al31 evaluated the efficacy of 0.1% adapalene. Adapalene 0. 1% produced numerically significant reduction of Grade 1 and Grade 2 lesions at each visit in a 12 weeks follow up study done by Pandi et al32 in India. (p< 0. 001). Adapalene has anti-inflammatory and keratolytic action within pilosebaceous duct.85 It reduces keratinocyte proliferation and differentiation.31 It normalizes the desquamation of the epithelium, inhibiting the formation of comedones and also prevents the appearance of new lesions.34

In Group B, the mean score of non-inflammatory lesions was 11.3 at the first visit (baseline), which was reduced to 8.1, 4.9 and 2.7 at the end of 4, 8 and 12 weeks respectively. The mean score of inflammatory lesions was 8.8 at the first visit, which was reduced to 5.1, 2.7 and 1.1 at the end of 4, 8 and 12 weeks respectively. Whereas the mean score of total lesions was 20.1 during the first visit, which significantly reduced to 13.3, 7.6 and 3.8 at the end of 4, 8 and 12 weeks respectively, compared to monotherapy with 0.1% adapalene. Significant reduction in all lesions were seen at each visit (p <0.001). The findings are similar to those of Sittart et al30 who reported signifacnt reduction of inflammatory and total lesions from 4th to 12th week (p< 0.001) with adapalene 0.1%/benzoyl peroxide 2.5% gel.

In this study, the difference in reduction of non-inflammatory, inflammatory and total lesions was found to be significant between Group A and Group B (p< 0.001). Significantly greater reduction (p< 0.001) of non-inflammatory, inflammatory and

total lesion counts were seen in patients receiving adapalene 0.1%/benzoyl peroxide 2.5% gel than in those receiving adapalene 0.1% gel in three 12-week trials in patients aged ≥ 12 years reported by Keating et al.35 Benzoyl peroxide has bactericidal against C. acnes on the skin and within the hair follicles. Also, topical BP has shown mild sebostatic effects in comedonal acne.6, 36 Combination of adapalene and benzoyl peroxide provides a significant adjunctive efficacy and local tolerance benefit.37 When use together, adapalene enhances the skin penetration of benzoyl peroxide thus improving its efficacy.33

This study showed that both adapalene and combination of benzoyl peroxide with adapalene yielded better results when treating mild to moderate acne. However, the efficacy of combination was found to be better in the clearance of the lesions.

CONCLUSION

Our study concluded that topical benzoyl peroxide with adapalene is more efficacious to treat mild to moderate acne vulgaris.

ABBREVIATIONS

A   Adapalene

BP   Benzoyl Peroxide

BPO/A   Benzoyl Peroxide with Adapalene

C/BPO   Clindamycin with Benzoyl Peroxide

DHEAS   Dehydroepiandrosterone

GAGS   Global Acne Grading System

HOD   Head of Department

IGA   Investigators Global Assessment

IL   Inflammatory lesion

KMCTH   Kathmandu Medical College and Teaching Hospital

MS   Microsoft Excel

NIL   Non-inflammatory lesion

OPD   Out Patient Department

OD   Once daily

SD   Standard Deviation

SGS   Simple Grading System

TLC   Total Lesion Counting

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