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Original Article

Comparison of safety of clindamycin (1%) - benzoyl peroxide (5%) combination gel with adapalene (0.1%) - benzoyl peroxide (2.5%) combination gel in treatment of mild to moderate facial acne vulgaris: A randomized prospective study

Wazeda Begum[1], Md.Mostafizur Rahman[2], Md.Maruf-Ur-Rahman[3], Md. Saiful Kabir[4]

[1]Registrar, Department of Dermatology & Venereology, Dhaka National Medical College, [2]Professor (cc), Department of Dermatology & Venereology, Dhaka National Medical College, [3]Associate Professor (cc), Department of Biochemistry, Dhaka National Medical College, [4]Prof & Head, Department of Dermatology & Venereology, Dhaka National Medical College

Abstract:

Background: Pathogenesis of acne vulgaris is complex and and multifactorial. Topical combination therapy can target multiple pathogenic mechanisms and therefore is currently recommended as the standard treatment of mild-to-moderate acne vulgaris. Various clinical studies have assessed the efficacy and safety of combination therapy for acne & demonstrated significantly greater and faster results with the combination therapy.

Objective: The aim of this study was to compare the safety of clindamycin (1%) - benzoyl peroxide (5%) combination gel with adapalene (0.1%) - benzoyl peroxide (2.5%) combination gel in treatment of mild to moderate facial acne vulgaris.

Methods: A prospective, randomized and comparative study was conducted on diagnosed cases of facial acne vulgaris attending outpatient department of Dermatology & Venereology, Dhaka National Medical College & Hospital, Dhaka. A total of 60 patients of acne were selected as per inclusion & exclusion criteria and randomly divided into two groups, 30 patients in group A and 30 patients in group B. Clindamycin (1%)- benzoyl peroxide (5%) combination gel was given for 12 weeks in the group A, while adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel was given to the group B patients for same duration. All the drugs were provided in the gel form. The safety of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up. Safety and tolerability were assessed through evaluations of facial tolerability and adverse events. At each visit, any adverse effects like dryness, desquamation, erythema, burning sensation and irritation noted. All parameters were compared between two groups. Quantitative data was expressed as mean±SD. Values of the different parameters was compared to see the difference between two groups by using Chi-square test (x^2). $p<0.05$ was considered as significant and $p>0.05$ was taken as non significant. 95% confidence limit was taken as the level of significance.

Results: In the present study, side effects were observed in 40% of study subjects in C/BPO group & 66.66% in A/BPO group. Side effects observed in C/BPO group were dry skin 10%, desquamation 6.7%, burning sensation 3.3%, erythema 0% & irritation 3.3%. In A/BPO group, side effects were dry skin 13.3%, desquamation 13.3%, burning sensation 10%, erythema 3.3% & irritation 3.3%. There was no statistically significant mean difference was found between two groups ($p>0.05$), indicating adverse events & cutaneous toleribility of C/BPO were similar to A/BPO combination gel.

Conclusion: Adapalene (0.1%) - Benzoyl peroxide (2.5%) combination gel & Clindamycin (1%) - Benzoyl peroxide (5%) combination gel both are well tolerated & having similar safety profile for the treatment of mild to moderate facial acne vulgaris.

Keywords: Acne vulgaris, Pilosebaceous units, Comedones, Papules, Pustules, Nodules, Safety profile.

Introduction:

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous units, characterized by seborrhea, comedones, erythematous papules, pustules, nodules, pseudocysts and, in some cases, scarring.[1] It is due to an increased sebum production, hypercornification of the pilosebaceous unit, colonization with Propionibacterium acnes and inflammation. It is the

most common dermatological disorder affecting approximately 85% of individuals between the ages of 12 and 24.[2] The characteristic lesions in acne are called comedones which are actually the noninflammatory lesions whereas the inflammatory lesions are papules, pustules and nodules.[3]

Acne vulgaris is one of the most common skin disorders having multifaceted pathogenesis. Most dermatologists agree that the choice of agents used to treat acne involves the integration of multiple factors such as the severity of lesions present, duration of disease, past and present response to therapy, and tendency for scarring and post inflammatory pigmentation. Therapy is therefore tailored to the individual patient depending on the nature and severity of their acne. A wide range of systemic and topical treatments are available, covering all disease variants . No single topical acne therapy is effective in treating all 4 of these pathogenic factors.[4]

Fixed-combination products are reported to be effective, well tolerated, and more convenient for patients than multiple individual agents, and by reducing the number of medications and applications, fixed-combination products may improve patient adherence and treatment outcomes.[5]

A number of fixed-combination topical products are available for the treatment of acne, including clindamycin- BPO combinations and adapalene-BPO combinations. The fixed combination of adapalene and BPO (A/BPO) is a retinoid-antimicrobial combination that has proven to be more effective than monotherapy with either component or placebo.[6] Local irritation, including erythema, peeling, dryness, burning, and itching, is the most common adverse effect of topical retinoids, although the potential for irritation appears to be lower with adapalene than with other retinoids such as tretinoin.[7,8] BPO can also cause local irritation,[9] but combining adapalene and BPO has a comparable safety and tolerability profile relative to adapalene alone.[6]

Various clinical studies have assessed the safety of combination therapy for acne. These studies demonstrate significantly greater and faster results with the combination therapy with similar safety profile than with the single agent alone. The present study is the first one study to compare the safety of clindamycin-benzoyl peroxide combination gel with adapalene- benzoyl peroxide combination gel in treatment of mild to moderate facial acne vulgaris in Bangladesh.

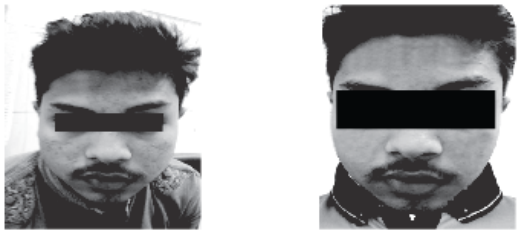
Materials & Methods:

A prospective, randomized and comparative study was conducted on diagnosed cases of mild to moderate facial acne vulgaris attending outpatient department of Dermatology & Venereology, Dhaka National Medical College & Hospital, Dhaka from June 2017 to Nov 2017.

It was an observational and open-label clinical trial in which both male and female patients in the age group of 12 to 35 years enrolled as per inclusion & exclusion criteria. Complete history, general physical examination and dermatological examinations were done after enrollment. The ethical clearance was obtained from the research advisory committee and Institutional Ethics committee. The study was started after obtaining written informed consent from each patient.

A total of 60 patients of acne were selected as per inclusion & exclusion criteria and randomly divided into two groups, 30 patients in group A and 30 patients in group B. Clindamycin (1%)- benzoyl peroxide (5%) combination gel was given for 12 weeks in the group A, while adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel was given to the group B patients for same duration. All the drugs were provided in the gel form. The safety of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up. Safety and tolerability were assessed through evaluations of facial tolerability and adverse events. At each visit, any adverse effects like dryness, desquamation, erythema, burning sensation and irritation were noted & were rated on a scale from 0 (none) to 3 (severe).

All parameters were compared between two groups. Quantitative data was expressed as mean±SD. Values of the different parameters was compared to see the difference between two groups by using student's t-test & Chi-square test (x^2). $p<0.05$ was considered as significant and $p>0.05$ was taken as non significant. 95% confidence limit was taken as the level of significance.



Before treatment (Group A) After treatment (Group A)

Fig-I: Evaluation of safty profile of C/BPO combination gel in treatment of mild to moderate facial acne vulgaris

Before treatment (Group B)

After treatment (Group B)

Fig-II: Evaluation of safty profile of A/BPO combination gel in treatment of mild to moderate facial acne vulgaris

Results:

Table:-I: Distribution of study subjects by age

Age Group	Group-A (C/BPO) (n=30)		Group-B (A/BPO) (n=30)	
	Frequency	Percent	Frequency	Percent
≤ 20 years	18	60	20	66.66
>20 years	12	40	10	33.34
Total	30	100	30	100
Mean ± SD	21.13± 6.95 (12-35)		20.26 ± 7.37 (12-34)	

Group A: Clindamycin (1%)- benzoyl peroxide (5%) combination gel (C/BPO)

Group B: Adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel (A/BPO)

Table-I: shows the age distribution of the study subjects. The mean age was 21.13± 6.95 years, ranging from 12-35 years in C/BPO group and in A/BPO group, the mean age was 20.26 ± 7.37 years, ranging from 12-34 years. In age group ≤ 20years, 18 (60%) patients belonged to C/BPO group & 20 (66.66%) patients belonged to A/BPO group. In age group >20 years, 12 (40%) patients belonged to C/BPO group & 10 (33.34%) patients belonged to A/BPO group.

Table-II: Distribution of study subjects by sex

Sex	Groups		
	Group-A (C/BPO) (n=30)	Group-B (A/BPO) (n=30)	Total
Male	13 (43.3%)	14 (53.3%)	27 (45%)
Female	17 (56.7%)	16 (46.7%)	33 (55%)
Total	30 (100.0%)	30 (100.0%)	60 (100.0%)

Table-II: shows the sex distribution of the study subjects. Among the total of 60 subjects, 27 (45%) were male and 33 (55%) were female. In C/BPO group, 13 (43.3%) were male and 17 (56.7%) were female and in A/BPO group, 14 (53.3%) were male and 16 (46.7%) were female.

Table-III: Side effects observed in the study

Safety	Group-A (C/BPO) (n=30)		Group-B (A/BPO) (n=30)	
	Number	Percent	Number	Percent
≤ With side effects	12	40%	20	66.66%
Without side effects	18	60%	10	33.34%

Table-III: shows side effects observed in group A(C/BPO) & group B (A/BPO). Side effects were observed in 40% of study subjects in C/BPO group & 66.66% in A/BPO group.

Table-IV: Distribution of study subjects by side effects

Side effects	Groups		P value
	Group A (C/BPO)	Group B (A/BPO)	
Dry skin	3 (10.0)	4 (13.3)	0.688^{ns}
Desquamation	2 (6.7)	4 (13.3)	0.389^{ns}
Burning sensation	1 (3.3)	3 (10.0)	0.301^{ns}
Erythema	0 (0.0)	1(3.3)	0.313^{ns}
Irritation	1 (3.3)	1 (3.3)	0.999^{ns}

ns=Non significant (P>0.05) ,***=P<0.001, **=P<0.01, *=P<0.05. Data were expressed as Mean±SD. Chi-square test was done to measure the level of significance.

Table-IV: shows different side effects observed in group A(C/BPO) & group B (A/BPO). Side effects observed in C/BPO group were dry skin 10%, desquamation 6.7%, burning sensation 3.3%, erythema 0% & irritation 3.3%. In A/BPO group, side effects were dry skin 13.3%, desquamation 13.3%, burning sensation 10%, erythema 3.3% & irritation 3.3%. There was no statistically significant mean difference was found between two groups (p>0.05), indicating adverse events & cutaneous toleribility of C/BPO were similar to A/BPO combination gel.

Discussion:

The present study was conducted to compare the efficacy and safety of clindamycin-benzoyl peroxide combination gel with adapalene- benzoyl peroxide combination gel in treatment of mild to moderate facial acne vulgaris. The patients only with mild to moderate (grade 1 and 2) acne vulgaris were included in the present study who were randomly divided into two groups, 30 patients in group A and 30 patients in group B. Clindamycin (1%)- benzoyl peroxide (5%) combination gel was given for 12 weeks in the group A, while adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel was given to the group B patients for same duration.The safety of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up. Safety and tolerability were assessed through evaluations of facial tolerability and adverse events. At each visit, any adverse effects like dryness, desquamation, erythema, burning sensation and irritation were noted.

In the present study, among the total of 60 subjects, 27 (45%) were male and 33 (55%) were female. In Group A (C/BPO), 13 (43.3%) were male and 17 (56.7%) were female and in Group B (A/BPO), 14 (53.3%) were male and 16 (46.7%) were female.

In this study, the mean age was 21.13± 6.95 years, ranging from 12-35 years in C/BPO group and in A/BPO group, the mean age was 20.26 ± 7.37 years, ranging from 12-34 years. In age group ≤ 20years, 18 (60%) patients belonged to C/BPO group & 20 (66.66%) patients belonged to A/BPO group. In age group >20 years, 12 (40%) patients belonged to C/BPO group & 10 (33.34%) patients belonged to A/BPO group. Similar results were obtained by the study of Cunliffe.[10]

Our study compared the adverse events & cutaneous tolerability or safety of clindamycin (1%) - benzoyl peroxide (5%) combination topical gel with adapalene (0.1%) - benzoyl peroxide (2.5%) combination gel in treatment of mild to moderate facial acne vulgaris.

In the present study, side effects were observed in 40% of study subjects in C/BPO group & 66.66% in A/BPO group. Side effects observed in C/BPO group were dry skin 10%, desquamation 6.7%, burning sensation 3.3%, erythema 0% & irritation 3.3%. In A/BPO group, side effects were dry skin 13.3%, desquamation 13.3%, burning sensation 10%, erythema 3.3% & irritation 3.3%. There was no statistically significant mean difference was found between two groups (p>0.05), indicating adverse events & cutaneous toleribility of C/BPO were similar to A/BPO combination gel. But this results disagree with the results of Lawrence Green et al.[11]They demonstrated that both products were well tolerated, but mean scores for erythema, dryness, and peeling were significantly higher with adapalene/benzoyl peroxide gel than with clindamycin/benzoyl peroxide gel at both Weeks 1 and 2 (p<0.03). Patients also rated clindamycin/benzoyl peroxide gel significantly more tolerable than adapalene/benzoyl peroxide gel for redness, dryness, burning, itching, and scaling at Weeks 1 and 2 (p≤ 0.0073). In our study, there was slightly higher adverse events with A/BPO group but it was statistically non significant. This results were consistent with the results of Zouboulis et al[12] they reported a greater incidence of local reactions with A/BPO but both A/BPO and C/BPO combination gel were well tolerated.

Conclusion

Adapalene (0.1%) - Benzoyl peroxide (2.5%) combination gel & Clindamycin (1%) - Benzoyl peroxide (5%) combination gel both are well tolerated & having similar safety profile. Both the topical combinations can be safely prescribed for the treatment of mild to moderate facial acne vulgaris.

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