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Original Article

Comparison of efficacy 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

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Abstract:

Background: Fixed-combination topical products are available for the treatment of facial acne vulgaris. The benefits of combined regimens include reduced risk of antibiotic resistance and improved treatment outcomes. Fixed-combination products are reported to be effective, well tolerated and more convenient for patients than multiple individual agents. Clindamycin- BPO combinations and adapalene-BPO combinations are recommended as standard treatment strategies in treating of mild to moderate facial acne vulgaris. Various clinical studies have assessed the efficacy of those topical combination therapy for facial acne vulgaris & demonstrated significantly greater and faster results.

Objective: The aim of this study was to compare the efficacy 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 aged 12 to 35 years, attending at outpatient department of Dermatology & Venereology, Dhaka National Medical College & Hospital, Dhaka from July 2017 to December 2017. 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 efficacy of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up by spot counting of acne lesions on the face. The number of inflammatory lesions (pustules, papules) and non inflammatory lesions (open and closed comedones) were noted during each visit in a separate chart for each patient. All parameters were compared between two groups. Quantitative data was expressed as mean±SD. Values of the different parameters were compared to see the difference between two groups by using unpaired t-test. $p<0.05$ was considered as significant and $p>0.05$ was taken as non significant. 95% confidence limit was taken as the level of significance.

Results: A/BPO combination gel were more effective in reducing total acne lesions including comedones, papules & pastules than C/BPO combination gel.

Conclusion: Adapalene (0.1%) - benzoyl peroxide (2.5%) combination gel is more effective than clindamycin (1%) - benzoyl peroxide (5%) combination gel in the treatment of mild to moderate facial acne vulgaris.

Keywords: Efficacy, Clindamycin, Benzoyl peroxide, Adapalene, Facial acne vulgaris.

Introduction:

Acne vulgaris is a chronic inflammatory dermatosis of the pilosebaceous unit characterized by open or closed comedones and inflammatory papules, pustules, nodules, or cysts.[1] Four major factors associated with the pathogenesis of acne are increased sebum production, follicular hyperkeratinization, Propionibacterium acnes proliferation, and inflammation. No single topical acne therapy is effective in treating all of these pathogenic factors.[2]

Topical combination therapy can target multiple pathogenic mechanisms and therefore is currently recommended as the standard of care in the treatment of mild-to-moderate acne, particularly in patients with an inflammatory component. The benefits of combined regimens include complementary mechanisms of action, reduced risk of antibiotic resistance, and improved treatment outcomes. An increasing number of antibiotic-retinoid and antibiotic-benzoyl peroxide combinations are now available.[3]

The Global Alliance to Improve Outcomes in Acne recommends the combination of a retinoid with an antimicrobial, preferably the non antibiotic benzoyl peroxide (BPO), as first-line therapy for mild-to-moderate acne. Topical antibiotics also have a role in acne management, but they should be used in combination with BPO to limit the development of P. acnes resistance.[3]

Adapalene is a receptor-selective naphthoic acid derivative with anti-inflammatory, comedolytic, and anticomedogenic properties.[4] The efficacy of adapalene in the treatment of acne vulgaris have been studied in numerous clinical trials.[5-6] Recent clinical studies investigating the efficacy of adapalene when used in combination with several antibiotics (oral lymecycline, oral doxycycline and topical clindamycin) for the treatment of inflammatory acne showed that the adapalene-antibiotic combinations were consistently more effective than antibiotic monotherapy.[7]

BPO is a safe and effective antimicrobial agent for the treatment of acne. It is a powerful antimicrobial agent destroying both surface and ductal bacterial organisms and yeasts. Its lipophilic properties permit penetration of the pilosebaceous duct and its efficacy it largely against superficial inflammatory lesions. It also has effects on non inflammatory lesions by reducing follicular hyperkeratosis to some degree. Benzoly peroxide formulations offer a useful approach in acne patients owing to their highly effective bactericidal effect. They are not associated with antimicrobial resistance and are active against fully sensitive and resistant stratins of Propionibacterium acnes.[7]

Clindamycin improves acne by reducing the levels of P. acnes and decreasing inflammation.[8] Combination therapy with clindamycin and benzoyl peroxide is a well accepted treatment regimen for mild to moderate acne as documented in clinical trials and meta-analysis reports. The advantages of this combination therapy are keratolytic action of benzoyl peroxide is possibly synergistic with the antibacterial activity of clindamycin and benzoyl peroxide may reduce chances of antimicrobial resistance to topical antibacterials like erythromycin and clindamycin.[8-9]

Various clinical studies have assessed the efficacy of combination therapy for acne. These studies demonstrate significantly greater and faster results with the combination therapy than with the single agents alone. Combinations of topical antibiotics plus topical benzoyl peroxide, topical retinoids plus topical or oral antibiotics, and topical retinoids plus topical benzoyl peroxide have all been investigated.[3] The present study is the first one study to compare the efficacy 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 at outpatient department of Dermatology & Venereology, Dhaka National Medical College & Hospital, Dhaka from July 2017 to December 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 efficacy of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up by spot counting of acne lesions on the face. The number of inflammatory lesions (pustules, papules) and non inflammatory lesions (open and closed comedones) were noted during each visit in a separate chart for each patient.10 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. $p<0.05$

was considered as significant and p>0.05 was taken as non significant. 95% confidence limit was taken as the level of significance.

Fig. : I Before treatment (Group A) After treatment (Group A)

Fig. : II Before treatment (Group B) After treatment (Group B

Results

Table-I : Number of Comedones in different follow up

Comedones	Groups		P-value
	Group A (C/BPO) (Mean ±SD)	Group A (A/BPO) (Mean ±SD)	
Baseline	13.20±1.78	12.83±1.96	0.453ns
1st follow up	10.06±2.33	11.03±2.60	0.136ns
2nd follow up	9.56±2.48	7.33±1.88	0.0001***
3rd follow up	7.23±1.83	5.40±1.45	0.0001***
Final follow up	4.83±1.26	2.73±1.55	0.0001***

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

Table: I shows number of Comedones in different follow up. The mean number of Comedones was 13.20±1.78 in C/BPO group & 12.83±1.96 in A/BPO group at base line. In 1st follow up mean number of Comedones were 10.06±2.33 & 11.03±2.60 in C/BPO group & A/BPO group respectively. There were no significant mean difference between two groups (P>0.05). In C/BPO group , mean number of Comedones were 9.56±2.48, 7.23±1.83 & 4.83±1.26 in 2nd, 3rd & final follow up respectively. In A/BPO group, the mean number of Comedones were 7.33±1.88, 5.40±1.45 & 2.73±1.55 in 2nd, 3rd & final follow up respectively. Significant mean difference were found (P< 0.001) between two groups, indicating A/BPO combination gel were more effective than C/BPO combination gel in treating comedones.

Table-II : Number of Papules in different follow up

Papules	Groups		P-value
	Group A (C/BPO) (Mean ±SD)	Group A (A/BPO) (Mean ±SD)	
Baseline	16.53±3.12	17.56±3.85	0.259ns
1st follow up	14.40±4.09	15.73±3.25	0.168ns
2nd follow up	13.53±5.11	11.63±4.39	0.128ns
3rd follow up	11.46±3.01	9.23±4.67	0.032*
Final follow up	9.16±4.29	6.26±2.13	0.001***

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

Table-: II shows number of Papules in different follow up. At base line mean number of Papules were 16.53±3.12 in C/BPO group & 17.56±3.85 in A/BPO group . In 1st follow up, mean number of Papules were 14.40±4.09 & 15.73±3.25 in C/BPO group & A/BPO group respectively. In 2nd follow up, mean number of Papules were 13.53±5.11 & 11.63±4.39 in C/BPO & A/BPO group respectively. There were no significant mean difference between two groups (P>0.05). In C/BPO group, mean number of Papules were 11.46±3.01 & 9.16±4.29 in 3rd & final follow up respectively. In A/BPO group, the mean number of Papules were 9.23±4.67 & 6.26±2.13 in 3rd & final follow up respectively. Significant mean difference was found between two groups, indicating A/BPO combination gel were more effective than C/BPO combination gel in treating Papules.

Table-III : Number of Pastules in different follow up

Pastules	Groups		P-value
	Group A (C/BPO) (Mean ±SD)	Group A (A/BPO) (Mean ±SD)	
Baseline	4.26±1.91	4.16±2.37	0.858ns
1st follow up	2.83±1.53	2.56±1.40	0.485ns
2nd follow up	1.83±0.91	1.73±0.73	0.643ns
3rd follow up	1.66±0.92	1.06±0.54	0.003*
Final follow up	1.56±0.72	0.70±0.55	0.0001***

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

Table-III : shows number of Pustules in different follow up. At base line mean number of Pustules were 4.26±1.91 in C/BPO group & 4.16±2.37 in A/BPO group. In 1st follow up, mean number of Pustules were 2.83±1.53 & 2.56±1.40 in C/BPO & A/BPO group respectively. In 2nd follow up, mean number of Pustules were 1.83±0.91 & 1.73±0.73 in C/BPO group A & A/BPO group respectively. There were no significant mean difference between two groups (P>0.05). In C/BPO group, the mean number of Pustules were 1.66±0.92 & 1.56±0.72 in 3rd & final follow up respectively. In A/BPO group, the mean number of Pustules were 1.06±0.54 & 0.70±0.55 in 3rd & final follow up respectively. Significant mean difference was found between two groups, indicating A/BPO combination gel were more effective than C/BPO combination gel in treating Pastules.

Table-IV : Mean of total acne score in different follow up

Pastules	Groups		P-value
	Group A (C/BPO) (Mean ±SD)	Group A (A/BPO) (Mean ±SD)	
Baseline	33.96±2.94	34.53±3.61	0.508ns
1st follow up	27.26±4.82	29.33±5.30	0.120ns
2nd follow up	24.93±6.37	20.66±3.03	0.002**
3rd follow up	20.33±3.45	15.66±3.98	0.0001***
Final follow up	15.56±3.77	9.63±2.15	0.0001***

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

Table-IV : shows the mean of total acne scores were 33.96±2.94 in C/BPO group & 34.53±3.61 in A/BPO group at base line. In 1st follow up, mean of total acne scores were 27.26±4.82 & 29.33±5.30 in C/BPO group & A/BPO group respectively. There were no significant mean difference between two groups (P>0.05). In 2nd follow up, mean of total acne scores were 24.93±6.37 & 20.66±3.03 in C/BPO group & A/BPO group respectively. In C/BPO group, the mean of total acne scores were 20.33±3.45 & 15.56±3.77 in 3rd & final follow up respectively. In A/BPO group, the mean of total acne scores were 15.66±3.98 & 9.63±2.15 in 3rd & final follow up respectively. Significant mean difference were found (P< 0.001) between two groups, indicating A/BPO combination gel were more effective in reducing total acne lesions than C/BPO combination gel.

Discussion

Pathogenesis of acne vulgaris is complex and and multifactorial which includes abnormal sebum production, follicular hyperkeratinization, bacterial proliferation and inflammation. So the treatment goals are directed to reduce activity of the sebaceous glands, normalize follicular proliferation, reduce bacterial colonization and control inflammation. There are different treatment options available for treatment of acne valgaris & all approaches have advantage and disadvantages.[11] But A/BPO and C/BPO combination gel are well tolerated & effective in reducing both inflammatory and non inflammatory acne vulgaris.[12-13]

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 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 efficacy of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up by spot counting of acne lesions on the face. The number of inflammatory lesions (pustules, papules) and non inflammatory lesions (open and closed comedones) were noted during each visit in a separate chart for each patient.

The present study revealed A/BPO combination gel were more effective in reducing total acne lesions including comedones, papules & pastules than C/BPO combination gel. Zouboulis et al.[14] performed a similar study and demonstrated that clindamycin/benzoyl peroxide combination (C/BPO) and adapalene/benzoyl peroxide (A/BPO) have comparable efficacy in the topical treatment of acne. Both treatments effectively reduced inflammatory, non inflammatory & total lesion counts over the 12 week treatment period. Based on data reported in the literature, Adapalene-BPO appears to induce similar magnitude of effect in reducing lesion counts relative to other available fixed-dose combinations, such as clindamycin-BPO.[15] In another study conducted by Langner et al.[16] concluded that benzoyl peroxide-clindamycin combination was found to have a significantly earlier onset of action, and was significantly more effective against inflammatory and total lesions. Gollnick H.P.M et al.[17] revealed that Adapalene-BPO have significantly greater & synergistic efficacy and faster onset of action with an acceptable safety profile in treatment of acne vulgaris. Our study comply with the results reported by Leyden et al.[18] who

evaluated the fixed-dose combination gel containing adapalene 0.1% and benzoyl peroxide 2.5%. They reported that this combination gel effectively inhibited both antibiotic-susceptible and antibiotic-resistant Propionibacterium acnes and reduced skin colonization by antibiotic-sensitive and antibiotic-resistant Propionibacterium acnes. This high effectiveness of the drug is due to potential synergistic effect of adapalene - BPO combination gel. A synergistic anti-inflammatory effect may result from BPO eliminating P. acnes and adapalene down regulating the cell surface receptor[19] (toll-like receptor 2) that P. acnes uses to induce inflammatory cytokine production. As a result, these two active ingredients could then synergistically decrease the impact of P. acnes in acne. In addition, the penetration of BPO is likely to be enhanced when combined with a adapalene, which alters the follicular microclimate.[2] Thiboutot et al.[3] & Diane M et al.[20] reported that the fixed-dose combination of adapalene and BPO provided significantly greater efficacy for the treatment of acne vulgaris as early as week 1 relative to monotherapies. But the results of our study disagree with the results of study conducted by Lawrence et al.[21] Several multicenter, double-blind, randomized and controlled studies demonstrated a favorable efficacy & safety profile of the combination gel of adapalene-BPO.[3]

Conclusion

From above discussion it may be concluded that adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel is more effective than clindamycin (1%) - benzoyl peroxide (5%) combination gel in the treatment of mild to moderate facial acne vulgaris.

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