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Comparative Study of Effectiveness of Clindamycin Monotherapy and Clindamycin - Benzoyl Peroxide Combination Therapy in Grade II Acne Patients

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ABSTRACT

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Background: Acne vulgaris is a chronic inflammatory disorder of pilosebaccous follicles affecting more than 85 percent of adolescents and young adults. Topical clindamycin inhibits Propionibacterium acnes and provides comedolytic as well as anti-inflammatory activity, in combination with Benzoyl Peroxide (BPO). Clindamycin in combination with benzoyl peroxide has been reported to reduce the emergence strains of Propionibacterium acnes that are less sensitive to antibiotics, which would help in optimizing efficacy in the management of mild to moderate acne vulgaris.

Aim: To compare the efficacy of combination of Clindamycin and Benzoyl Peroxide versus Clindamycin alone in the treatment of mild to moderate acne vulgaris in grade II acne patients.

Methods: Eighty patients were randomly allocated in to two groups of 40 each to receive topical Clindamycin (Group A) and Clindamycin-Benzoyl Peroxide (Group B), with evaluation at 2nd, 4th and 6th week follow up. Efficacy parameters of Non-Inflammatory and Inflammatory lesion count and safety parameters such as erythema, dryness, burning and pruritis were also measured. Dermatologist perception along with patient's response towards the treatment was also observed.

Result: Mean age of the patients was within the age group of 21-25 years. Females constituted about 77.5% and 22.5% were males. Clindamycin showed 25.05% and 28.4% improvement and Clindamycin-Benzoyl Peroxide combination showed 75.17% and 78.3% improvements in Non-Inflammatory and Inflammatory lesion counts. Erythema, dryness, burning and pruritis were observed in both the groups, and was gradually reduced by week 6.

Conclusion: Our data suggested that, Clindamycin-Benzoyl Peroxide combination is an effective topical agent in the treatment of patients with mild to moderately acne.

Keywords: Acne, efficacy, safety, Clindamycin-Benzoyl peroxide, Monotherapy, Combination Therapy, Non-Inflammatory, Inflammatory lesion count.

INTRODUCTION

Acne is a common, chronic inflammatory disorder of the pilosebaceous unit in which a microcomedo develops as an initial condition and the most common form of acne is acne vulgaris. Other variants of acne are neonatal acne, adult acne, acne cosmetica, and acne mechanica. These descriptors refer to age of onset or causative factors. Localization of acne vulgaris on the facial area, especially in an adolescent population, significantly impacts self-esteem. Although acne is self-limiting, it can persist for years and can result in disfigurement and scarring. While acne does not affect the health overall, it impact one's emotional well-being and function can be critical and are associated with depression, anxiety and higher-than-average unemployment rates[1]. Other factors influencing acne including diet, menstruation, hormonal changes, environment and stress.[2]

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The precise mechanisms of acne are not known but there are four major pathogenic factors: increased sebum production, hypercornification of pilosebaceous duct, abnormal bacterial function and production of inflammation[3].

Acne is often categorized into 4 grades according to the degree and severity of lesions:

Grade-I: There is a predominance of non-Inflammatory lesions or comedones both open and closed but there may also be a few small inflammatory lesions papules or pustules. *Grade-II:* Acne consists of comedones, papules and pustules the lesions are mainly limited on the face. *Grade-III*: Acne has involvement of the upper trunk and shoulders with numerous papules and pustules and few larger lesions. *Grade-IV*: Acne consists of large painful cystic lesions which are usually on the face and upper trunk.[4]

Topical preparations constitute the sole treatment in many patients with acne vulgaris and are a part of therapeutic regimen in almost all patients. Although topical treatment is enough for comedonal acne, in case of more severe acne, topical treatment can be combined with systemic treatment. Topical treatment of acne vulgaris has changed over the years,

with the most popular topical agents in use being the retinoids, benzoyl peroxide, azelaic acid, and topical antibiotics.[5]

Topical antimicrobial agents are commonly used as first-line agents for the management of mild to moderate acne vulgaris. Agents with antibacterial activity, such as benzoyl peroxide and clindamycin reduce counts of Propionibacterium acnes, while also decreasing the number of inflammatory and non-Inflammatory lesions. In order to optimize efficacy, topical antibiotics are most commonly used in combination with benzoyl peroxide, an approach which also reduces the emergence of strains of Propionibacterium acnes that are less sensitive to antibiotics. This wide array of options allows dermatologists to tailor topical treatments to the needs of individual patients.[6]

The current clinical study is proposed to assess the efficacy and safety of combination therapy (Clindamycin and Benzoyl Peroxide) over monotherapy (Clindamycin) for acne treatment in grade-II acne patients.

MATERIAL AND METHODS

A randomized open label study was conducted for nine months to assess the efficacy of topical Clindamycin monotherapy based on the treatment outcome and to evaluate the therapeutic efficacy of Clindamycin –Benzoyl Peroxide combination therapy over Clindamycin monotherapy. Institutional ethical clearance was obtained prior to the study. All the participants who gave the informed consent were included in the study.

Patients of either sex aged 12 to 30 years, with more than 5 inflammatory facial lesions(papules, pustules and comedones white and black head) and acne severity grade II were included. Any other topical medication and cosmetics was listed as concomitant medication.

Exclusion criteria: Pregnant or lactating women, patients suffering from Acne conglobata, Acne fulminans or secondary acne and Grade I, Grade III and Grade IV, patients on oral/injectable steroids, anti-epileptic, anti-tuberculosis and anti-psychotic drugs, patients with known renal or hepatic disease known or suspected allergy to lincomycin were excluded from this study along with patients with history of adverse response to benzoyl peroxide or to any components of formulations.

A total of eighty patients were enrolled in the study, among which 40 patients received Clindamycin monotherapy (Group-A) and 40 patients received Clindamycin-Benzoyl Peroxide combination therapy (Group-B). Demographic data which included age, sex, education level and place of stay was collected, and clinical data was collected using a patient profile form and clinical examination was done to confirm diagnosis. Treatment was continued for 6 consecutive weeks. The application of study medication was initiated at baseline visit (day one) and follow-up visits were conducted on 2nd, 4th, and 6th week. Patients were instructed not to take any other anti-acne treatment during the study such as systemic antibiotics and corticosteroids, as well as any treatment likely to interfere with Clindamycin and Benzoyl Peroxide. Patients were educated to apply a thin layer of gel to the face twice daily morning and in the night before going to bed in case of monotherapy and for combination therapy-Clindamycin in the morning and Benzoyl Peroxide in the night before going to bed. The patient were additionally instructed to avoid exposure to the sun, to avoid the use of cosmetics other than eye and lip makeup (for women) and after shave products or colognes (for men).

Clinical assessment:

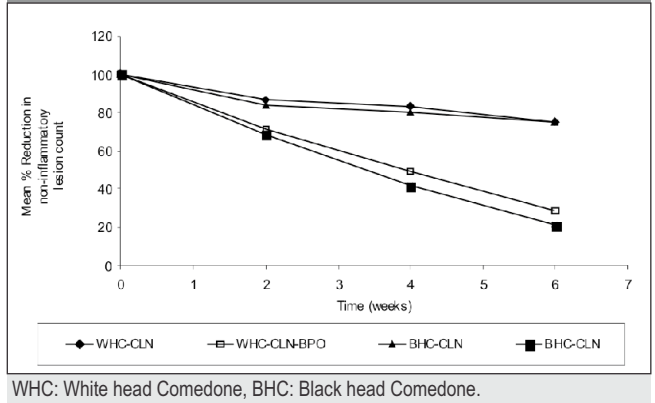
Lesion count, broken down into non-inflammatory lesion (open/closed comedones) and inflammatory lesions (papules, pustules) were evaluated from the face, including forehead, cheeks and chin at baseline for inclusion followed at week 2, 4 & 6. Demographic data, medical history, previous treatment data and baseline disease data were also collected during the enrollment.

Other symptoms like erythema, dryness, burning and pruritus were noted at baseline and at follow up on a 5 point scale after examination of the area involved (0=none, 1=slight, 2=mild, 3=moderate, 4= severe).

RESULTS

A total of eighty patients were enrolled and all participated in the 9 months study, which included 18 males and 62 females. Mean age of the participants was 21.73 years in both the groups with female patients showing a higher incidence of acne than men. Education pattern revealed that higher number of participants were graduates and residing in the urban area.

Fig. 1: Mean percent reduction in non-inflammatory lesion count.



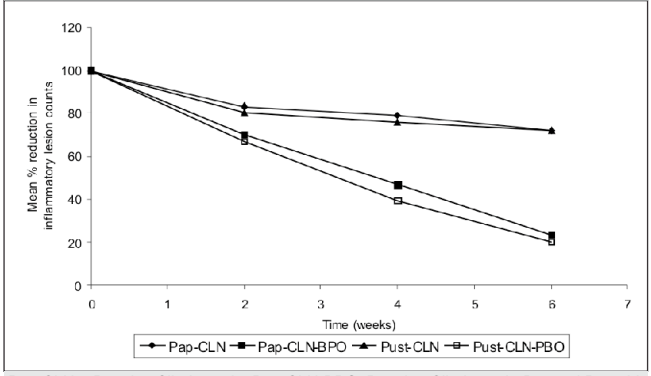
WHC: White head Comedone, BHC: Black head Comedone.
CLN-BPO: Clindaycin –Benzoyl Peroxide, CLN: Clindamycin.

Reduction in non-inflammatory and inflammatory lesion count: Comparison of Non-Inflammatory and Inflammatory lesion count reduction from the baseline (Figure no. 1) show a significant reduction in lesion count from baseline to 6th week.

Non-inflammatory lesion count as assessed by comedone white head and comedone black heads did show a significant reduction. The number of comedones white head in group A at baseline was 10.05 ± 3.45 and reduced to 7.55 ± 4.95 at 6th week, whereas in group B it was reduced to 2.73 ± 1.63 from the baseline value of 9.60 ± 3.13. Similarly reduction of comedone black heads was seen in group B which showed a significant reduction from 6.50 ± 1.92 to 1.38± 1.08 ($P < 0.001$).

Inflammatory lesion counts as assessed by the presence of papules and pustules also showed a significant reduction at the 6th week. Number of papules in group B was decreased to a greater extent from 6.13± 1.60 (baseline) to 1.43± 1.03 (6th week) in comparison to group A which reduced from 5.48 ± 2.00 to 3.93 ± 2.73 (6th week) with $P < 0.001$. Number of pustules also reduced to higher extent in group B (5.18 ± 1.63 to 1.05 ± 0.98 at 6th week) in comparison to group A (3.88 ± 1.56 to 2.78± 2.02 at 6th week).

Fig 2: Mean percent reduction in inflammatory lesion count.



Pap-CLN :- Papules Clindamycin, Pap-CLN-BPO: Papules-Clindamycin-Benzoyl Peroxide
Pus-CLN: Pustules-Clindamycin, Pust-CLN-BPO: Pustules-Clindamycin-Benzoyl Peroxide

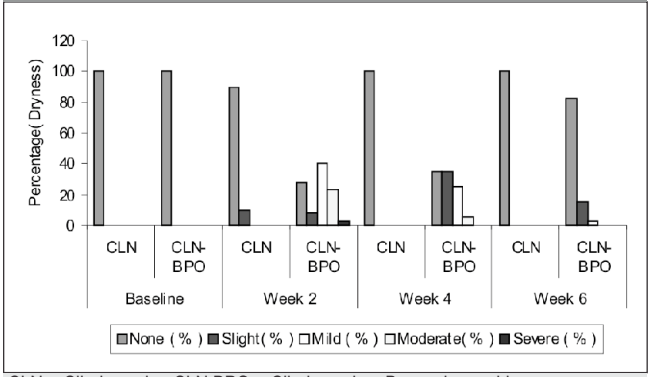
Table 1: Demographic characteristics of study participants

Variables	Group A (CLN)N (%)	Group B (CLN-BPO)N (%)
Gender		
Male	8 (20%)	10(25%)
Female	32(80%)	30(75%)
Age (years±S.D.)	21.73± 4.37	21.73± 3.84
Education level		
Primary	4(10%)	2(5%)
Secondary	10(25%)	25(20%)
Graduate	26(65%)	70(54%)
Region of stay		
Rural	6(15)	10(25%)
Urban	34(85)	30(75%)

Side effects of Clindamycin and Clindamycin –Benzoyl Peroxide therapy were assessed by measuring erythema, dryness, burning and pruritis. Assessing the side effects, it was observed that both monotherapy and combination therapy caused more of burning and dryness (Fig 3&4 respectively), but more number of cases was seen in group B patients than group A patients. At week 2 groups A, 1(2.5%) patient and in group B 8(20%) patients had mild burning, however at the end of week 6, only group B 17(42.5%) patients reported of slight burning. [Fig: 4]

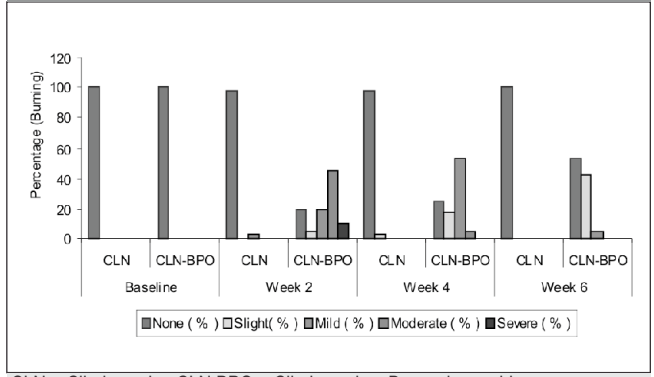
At week 2, in group A 4(10%) patients had slight dryness and in group B, 16(40%) patients had mild dryness. At the week 6 only group B, 1(2.5%) patient had mild dryness (Fig: 3) Similarly pruritis was more in group B patients than group A, whereas erythema is seen in both the groups at baseline and 2nd week but reduced at subsequent weeks. In patients having increased burning, the concentration of Benzoyl Peroxide was reduced to 2.5% from 5% Benzoyl Peroxide(Fig: 4). However, the side effects observed were not so severe; hence the therapy was still continued.

Fig. 3: Tolerability assessment: dryness



CLN :- Clindamycin, CLN BPO :- Clindamycin – Benzoyl peroxide.

Fig 4: Tolerability assessment: Burning



CLN :- Clindamycin, CLN BPO :- Clindamycin – Benzoyl peroxide.

DISCUSSION

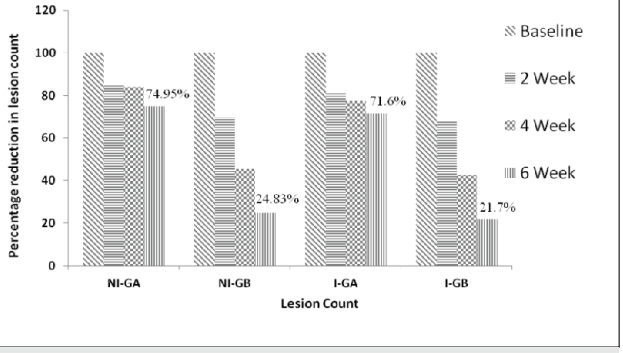
Acne vulgaris is the most common dermatologic condition affecting adolescents and young adults, successful acne therapy is the primary requirement to lessen the psychological distress associated with acne

In our study, the safety and efficacy of combination therapy over monotherapy was assessed mainly in grade II acne patients for 6 weeks. It was seen that patients of both sexes were affected with acne, but to a greater extent in females. As reported[7] by Valia R et al, acne developes earlier in females than in males. We also observed that most of the study participants did not have any past medication history for treating acne except that some of them used home remedies to manage acne.

Our study suggests that combination therapy of clindamycin-benzoyl peroxide offers a higher efficacy and good tolerability over monotherapy of clindamycin, which is evident from the reduction in lesion counts. Clindamycin showed 25.05% and 28.4% improvement, which was evaluated by the reduction in Non-Inflammatory and inflammatory lesion counts respectively. Whereas in Clindamycin-Benzoyl Peroxide combination showed 75.17% and 78.3% improvements in reducing non-Inflammatory and nflammatory lesion counts (Fig:5).

Recent research suggests that the benzoyl peroxide free radicals are more highly active in the presence of a chemical compound that possesses a tertiary amine within its structure, including the antibiotics clindamycin and erythromycin, benzoyl peroxide penetrates comedones and microcomedones, which exposes the bacteria to higher concentrations of both more benzoyl peroxide and the antibiotic[8].

Fig. 5: Comparison of reduction in Non-inflammatory & Inflammatory lesions count from baseline to week 6.



NI-GA :- Non- inflammatory lesion count group A.
NI-GB :- Non- inflammatory lesion count group B.
I-GA :- Inflammatory lesion count group A.
I-GB :- Inflamatory lesion count group B.

Side effects as assessed by erythema, dryness, burning and pruritis were observed in both the groups, it was gradually reduced by week 6. However, the severity of side effects was very low which helped in further continuation of therapy.

Assessment of response by the dermatologist and also the patient perception to treatment revealed satisfication towards the outcome of therapy with marked improvements in group B receiving combination therapy in comparison to group A (clindamycin monotherapy) who had mild improvements. Nevertheless, studies have suggested that the use of benzoyl peroxide in combination with the aforementioned antibiotics may prevent the development of antibiotic resistance as well as improve the clinical manifestations of Acne vulgaris in those who have already developed antibiotic resistance[9].

The limitation of the present study was that the study did not involve other grade patients like I, III and IV and was done only for facial acne not include chest, arms and back trunk.

Future research should require for comparison of study drugs with other anti-acne therapies and also assess the quality of life of acne patients using DLQI (Dermatology life quality index Questionnaire).

CONCLUSION

Overall outcome of the study indicates that Clindamycin –Benzoyl peroxide combination has more therapeutic efficacy when compared to Clindamycin monotherapy which is evident from the percentage improvement. Clindamycin-Benzoyl peroxide combination showed three fold improvement in Non-inflammatory and Inflammatory lesion count reduction in comparison to monotherapy. This marked difference proves the superiority of Clindamycin-Benzoyl peroxide combination which can be visible as early as week 2 from initiation of therapy.

Thus, Clindamycin-Benzoyl Peroxide combination is an effective topical agent in the treatment of patients with mild to moderately severe acne. It is a suitable alternative for patients who are currently using topical antibacterials alone or in conjunction with other topical anti-acne agents or systemic antibacterials.

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