



## Observational study to see efficacy and Safety profile of Benzoyl peroxide 2.5%, Adapalene 0.1% and its fixed dose combination in mild to moderate grade of Acne Vulgaris

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### Abstract

**Introduction:** Topical therapies are indicated for mild to moderate cases of acne vulgaris. The most commonly used are benzoyl peroxide 2.5% gel and adapalene 0.1% gel. Combination of both BPO-Adapalene in a gel has excellent results with no major side effects and no risk of resistance like antibiotics.

**Aim:** This study was undertaken to find out the efficacy and safety profile of Benzoyl peroxide-adapalene fixed dose topical combination therapy relative to benzoyl peroxide and adapalene monotherapy in patients of acne vulgaris.

**Material & Method:** In this comparative study of 90 patients of either sex, aged 12 years or more, with mild to moderate grade of Acne Vulgaris and with lesions restricted over the face were enrolled and were divided into three different groups of 30 each by sealed envelope method. Group A-patients were treated with BPO 2.5% gel, Group B- with adapalene 0.1% gel and Group-C were treated with BPO-Adapalene combination gel. Single night time application of gel was advised to patient for a period of 12 weeks. The patients were followed up at 0, 2, 4, 8, 12 weeks at each visit. The decrease in the total number of (both inflammatory + non-inflammatory) lesions and side effects were noted.

**Results:** At the end of the 12 weeks treatment, all groups showed significant improvement. The decrease in mean lesion count of group A, group B and group C was 52.6%, 55.2%, and 78.4% respectively at 12<sup>th</sup> week. Group C had excellent results with better tolerability. Dryness was a common side effect.

**Conclusion:** Fixed dose combination of adapalene-benzoyl peroxide has greater efficacy for treatment of acne vulgaris with comparatively lesser side effects than monotherapies.

**Keywords:** Acne vulgaris, Benzoyl Peroxide, Adapalene, BPO-Adapalene, efficacy, side effects.

### Introduction

Acne is ubiquitous and with varying degrees of severity, affects approximately 85% of individuals at some time between the ages of 12 and 24 years<sup>1</sup>

Acne is chronic inflammatory disease of the pilosebaceous units, characterized by seborrhea, the formation of comedones, erythematous papules, pustules, nodules, pseudocysts and in

some cases scarring predominantly present on face, back and chest.<sup>2</sup> It has complex aetiology, involving abnormal keratinization, hormonal dysfunction, bacterial growth and immune hypersensitivity.<sup>3-4</sup> Acne varies enormously in its clinical signs, aetiology and severity, so accordingly, the treatment option varies to the severity grades of the disease.

Conventional topical therapies recommended for the treatment of acne vulgaris include Antibiotics (Erythromycin, Clindamycin), Retinoids (Adapalene, Tretinoin), Benzoyl peroxide (BPO), Salicylic acid and Azelaic acid. Due to the multifactorial pathogenesis of acne vulgaris and the limitations of the conventional topical therapies, combination therapy using agents with complementary mechanisms provides the opportunity to target multiple pathogenic causes of acne vulgaris.<sup>5</sup>

Adapalene is a receptor-selective naphthoic acid derivative with anti-inflammatory, comedolytic, and anti-comedogenic properties and is thought to be very stable when combined with antimicrobial agent.<sup>6-11</sup> Benzoyl peroxide release free oxygen radicals and oxidize bacterial proteins and is effective over inflammatory lesions with rapid bactericidal action.<sup>12</sup>

Hence, this combination may be expected to decrease the incidence of bacterial resistance relative to antibiotics.<sup>13</sup> Furthermore, unlike tretinoin, adapalene is stable when combined with BPO, even in the presence of light.<sup>14</sup>

### Material & Methods

After prior approval from the Institute Ethics Committee the study was initiated. A total of 90 patients of either sex, aged 12 years or more, with mild to moderate grade of Acne Vulgaris and with lesions restricted over the face were included in the study. Pregnant and lactating females, patients with known hypersensitivity to drug and patients with severe grade of acne were excluded in study. Prior written consent was taken and patients were divided into three groups of 30 patients each- A, B and C by sealed envelope method. Group A- was

treated with Benzoyl peroxide 2.5% gel as monotherapy, Group B- with Adapalene 0.1% gel as monotherapy and Group C- with BPO and adapalene combination gel. The patients were instructed to apply gel at night time for 12 weeks. Efficacy was observed by calculating decrease in total mean percentage of lesions, along with the change in severity in grade of acne by Investigator's Global Scale on week 0, 2, 4, 8, 12. Data was collected and entered into Microsoft excel (MS Office XP) and Master Chart was prepared. The data were analyzed using SPSS software version 18.0. Results were calculated at 12<sup>th</sup> week. Side effects like erythema, scaling, dryness and burning were also recorded on each visit.

### Investigator's Global Assessment Scale (IGA)

0	Clear	Residual hyperpigmentation, erythema may be present
1	Almost Clear	A few scattered comedones and a few small papules
2	Mild	Easily recognizable: less than half the face is involved. Some comedones and some papules and pustules.
3	Moderate	More than half of the face is involved. Many comedones, papules and pustules. One nodule may be present
4	Severe	Entire face is involved, covered with comedones, numerous papules and pustules and few nodules and cysts

### Results

In this prospective, observational study of 90 patients on treatment of Acne Vulgaris who fulfilled the inclusion and exclusion criterion showed that maximum number of patients were females in the age group of 12-21 years. Mean age group of patients in group A, B and C was 20.53, 19.07 and 19.90 respectively. Most of the patients were from urban area.(Table I)

Table II, shows total mean lesion count at week 0 and 12. Figure- 1 shows Decrease in mean of total lesion count which was 52.6%, 55.2%, 78.4% for group A, B and C respectively. A positive reduction in both inflammatory lesion counts and non-inflammatory lesion counts were seen at 12<sup>th</sup> visit. Percentage change in inflammatory lesions in combination group was maximum (76.78%) as compared to benzoyl peroxide group (60.59%)

and adapalene group (56.41%). Similarly, percentage change of non-inflammatory lesions was also maximum in combination group (78.37%) as compared to benzoyl peroxide (47.63%) or adapalene monotherapy (54.51) as shown in Figures 2-3.

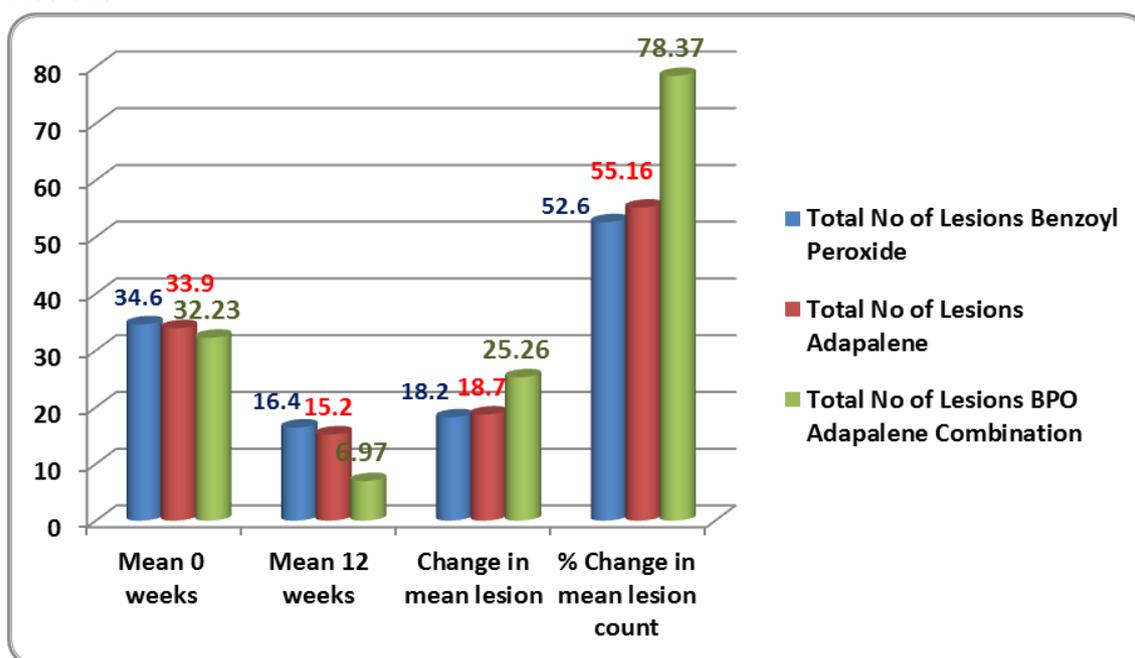
In total, the combination therapy regimen consistently provided significant decrease in total, inflammatory and non-inflammatory lesions. This difference was statistically significant ( $< 0.05$ ). A decrease was observed in total lesion counts, inflammatory and non-inflammatory lesions observed as early as the first post baseline assessment but that was not statistically significant.

IGA Scale of acne grading at baseline and 12 weeks is shown in Table III, in which patients

who got 'clear or almost clear' that is grade 0 and grade 1 of IGA at week 12 were 33.3%, 30% and 46.6% in group A, B, C respectively. So, maximum number of patients cleared with the combination of benzoyl peroxide and adapalene, (Figure 4) however, this difference was statistically not significant.

Safety evaluation was also done at every visit of therapy. Total number of adverse events in Benzoyl peroxide group was 9(30%) followed by 13(44%) adverse events in BPO group. Total adverse events in BPO-adapalene combination were also 13(44%). Dryness was predominant side effect amongst all groups which decreased on continuing of treatment.

**Figure 1:** Distribution of patients with Acne: Improvement in clinical condition with weeks in view of Mean total no. of lesions.



## Discussion

Acne vulgaris is a chronic inflammatory disease of adolescence and young age, age group was found appropriate for the disease in this study. Due to its complex pathogenesis, the multifactorial effects are demanded from acne therapy for which often combination therapy is recommended.<sup>15-16</sup>

Combination therapy like benzoyl peroxide and adapalene is a rare and very effective combination as benzoyl peroxide is lipophilic and when applied to the skin it is capable of penetrating into the pilosebaceous follicle. Within the skin, benzoyl peroxide releases free radical oxygen and benzoic acid. The free radicals oxidize bacterial proteins.<sup>12</sup> It is effective in acne because it provides good efficacy over inflammatory lesions,

with rapid bactericidal action. Whereas adapalene is a receptor-selective naphthoic acid derivative with anti-inflammatory, comedolytic, and anti-comedogenic properties.<sup>6-10</sup> It is recognized as an effective topical retinoid with a favorable tolerability profile<sup>11</sup> and is therefore a rational selection for combination therapy with an antimicrobial agent.

The fixed-dose combination of adapalene 0.1% and BPO 2.5% for the treatment of acne combines two agents with different modes of action to address multiple pathophysiological factors of acne. The aim of the current study was to evaluate the efficacy and safety of the adapalene-BPO combination relative to the individual monotherapies in mild to moderate grade of Acne Vulgaris. Result of the present study demonstrate a significant reduction in both inflammatory and non-inflammatory lesions. Mean decrease in total lesions BPO, Adapalene and Combination therapy is 52.6%, 55.2%, 78.4% respectively at 12 th week. Similarly progressive reduction with combination therapy in acne severity was seen on IGA Scale and success rate was calculated with higher percentage as compared to monotherapies. Similarly in several double-blind, randomized controlled trials.<sup>17-19</sup> The adapalene-BPO combination therapy applied once daily for 12 weeks significantly reduced the number of both inflammatory and non inflammatory lesions in subjects with mild and moderate acne vulgaris, with a rapid onset of action and a good safety profile when compared with the adapalene and BPO monotherapies. The effect of A-BPO was sustained for 4 months, and was safe as a long-term treatment for up to 12 months.<sup>20</sup>

It was found that total number of adverse events in Benzoyl peroxide group was 9(30%) followed by 13(44%) adverse events in BPO group. Total adverse events in BPO-adapalene were also 13(44%).

Common side effects amongst all groups were erythema, burning, scaling, and dryness. Out of all dryness was seen maximum in adapalene-BPO group with 8 patients.

To conclude, all the three topical therapies i.e. Benzoyl peroxide 2.5% gel, Adapalene 0.1% gel and combination gel (Adap-BPO) are effective in the management of Grade 2 and Grade 3 (Mild-Moderate) acne. However combination therapy was found to be significantly superior to monotherapies. Fixed-dose combination products can offer several benefits for physicians and their patients. They eliminate the guess work involved regarding the timing of application of topical products as well as concerns regarding stability and chemical compatibility of two separate formulations. Beyond the enhanced efficacy of utilizing two agents with synergistic and complementary pharmacological properties, the use of fixed-dose combinations may be more convenient and simplify the treatment regimen, thereby potentially improving treatment adherence and outcomes.

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**Ethical clearance--** Taken

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