



Original Research Article

Evaluation of safety and efficacy of hydrogen peroxide stabilized cream for treatment of mild to moderate acne vulgaris in comparison with benzoyl peroxide gel - double blinded, randomized control study

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ABSTRACT

Acne is defined as a chronic inflammatory disorder of the pilosebaceous unit, which is characterized by comedones, seborrhea, pustules, nodules, pseudocysts and scarring, in some cases. Benzoyl peroxide (BP) is a time tested molecule in the management of acne. In current study we have tried to compare efficacy of benzoyl peroxide with hydrogen peroxide (HP) in acne vulgaris (AV).

Aims : To study efficacy and local tolerability of BP and HP in Acne Vulgaris treatment. To compare the efficacy and local tolerability of BP gel and HP cream in a Acne Vulgaris (GRADE 1 AND 2) treatment.

Materials and Methods: A double blinded, randomised control study for the duration of 18 months was carried out in which a total of 150 patients of acne vulgaris (Grade 1 & 2) between the age of 13-30 years of both genders were recruited, which were divided in two groups, with one group treated with benzoyl peroxide gel 2.5% and second group being treated with hydrogen peroxide cream. All the data analysis was done using IBM SPSS ver. 20 software.

Results: Both drugs were found to be equally efficacious in reducing acne lesions. Hydrogen peroxide group experienced less side-effects as compared to benzoyl peroxide group.

Conclusion: Hydrogen peroxide and benzoyl peroxide are equally efficacious.

Key Messages: In acne grade one and two benzoyl peroxide and hydrogen peroxide are equally efficacious though hydrogen peroxide has less adverse effect.

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1. Introduction

Acne is the commonest dermatological disorder affecting 85% of individuals in age group of 12 and 24 years.¹ It is estimated that in age group of 25 to 40 years 41% of people suffer from acne lesions for at least 3 to 4 months per year.²

Current treatments include oral medications and topical that counteract sebum production, P. acne colonization and inflammation.³ Widely used topical compounds are benzoyl peroxide⁴ (BP), antibiotics⁵ and retinoids⁶ while antibiotics like tetracyclines, azithromycin,⁷ retinol derivatives like isotretinoin⁸ and oral contraceptives

like cyproterone acetate are commonly used oral agents.⁹

According to the first global alliance therapeutic guidelines of acne (2003), (BP) was considered the first drug of choice for treatment of mild and moderate AV.¹⁰ This statement was substantially confirmed in the second global alliance publication in 2009.¹¹

Recently, a new formulation of Hydrogen peroxide 1% (HP) in stabilised cream became available in Indian market. The study product contained hydrogen peroxide (H₂O₂), which is an odourless and colourless liquid.¹² HP is very unstable and disintegrate upon light exposure, but dissolves easily in water.¹³ The stabilization of HP in the dermo-cosmetic formulations was extremely difficult, which required addition of stabilizing agents and

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aspecialized packaging.¹⁴

In present study we tried to evaluate the safety and efficacy of HP stabilized cream for treatment of mild to moderate AV in comparison with BP gel.

2. Materials and Methods

We conducted a double blinded, randomised control study for the duration of 18 months from November 2016 to May 2018.

Sample size was calculated by using the formula $4pq/D^2$ where p is prevalence and q is 10-p and D^2 is allowable error. Simple random sampling method was used for randomisation. A total of 150 consenting patients of acne vulgaris (Grade 1 & 2) between the age of 13-30 years of both genders were recruited during this time period and minors' consent was taken from parents.

After ethical approval data collection was started and patients were divided randomly in two groups, with one group treated with benzoyl peroxide gel 2.5% and second group being treated with hydrogen peroxide cream, having 75 patients in each group respectively. Both investigator and the patient were blinded to the type of treatment.

Efficacy were assessed at each visit (baseline, week 4, and week 8) by counting total lesion (TL), IL, NIL and by taking photographs at baseline, 4 week, 8 week. At 8 week, a clinical global assessment, in comparison with baseline were performed using qualitative score: 0 = worsening, 1= no improvement, 2=mild improvement, 3=moderate improvement, 4=good improvement, 5= very good improvement. Tolerability were assessed at 4 and 8 week on 0 – 3 qualitative scale 0= poor tolerability, 1=mild tolerability, 2=moderate tolerability, 3=good tolerability. Side effects like erythema, dryness, burning sensation and itching were evaluated using 0-3 qualitative score 0= none, 1=mild, 2=moderate, 3=severe

To assure the blinded characteristics of the trial, the observer was unaware of the treatment allocation performed. The observer only took photographs and calculated total number of lesion and assessed tolerability on the basis of pre- structured performa at baseline and at each visit.

Statistical Analysis

All the data analysis was done using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was used to prepare tables. Microsoft word 2010 was used to prepare graphs. Different study variables were compared using Chi square test. Value of less than 0.05 was considered statistically significant.

3. Result

Majority of the patients were in the age group of 16-20 years [65 (43.3%)] followed by 21-25 years [39 (26%)]. Majority of the patients were of young age (<25 years). Most of the

patients were female [91 (60.7%)].

Majority of the patients had acne grade 2 [81 (54%)] followed by acne grade 1 [69 (46%)].

Maximum patients had acne on the cheek [57 (38%)] followed by forehead, Chin and Cheek.

Comparing inflammatory lesions, non inflammatory lesions and total lesions at follow up with baseline revealed that both the treatment were equally efficacious in reducing the inflammatory lesions, non inflammatory lesions and total lesions at the end of 4th and 8th week ($p > 0.05$). (Figures 1, 2 and 3).

In present study comparing the tolerability of both the drugs revealed that erythema was significantly higher with benzoyl peroxide (7 out of 8 cases) as compared to hydrogen peroxide (1 out of 8 cases). Similarly, Pruritus and Burning Sensation were significantly higher among the patients using benzoyl peroxide (9 out of 10 cases) and (10 out of 11 cases) as compared to hydrogen peroxide (1 out of 10 cases) and (1 out of 11 cases) respectively. (Figure 4)

Comparing both treatment for total lesions after 8th week of treatment between grade 1 and 2 of acne, we found both the drug equivalent. That means both the drugs are equally efficacious for grade 1 and grade 2 of acne (P value > 0.05).

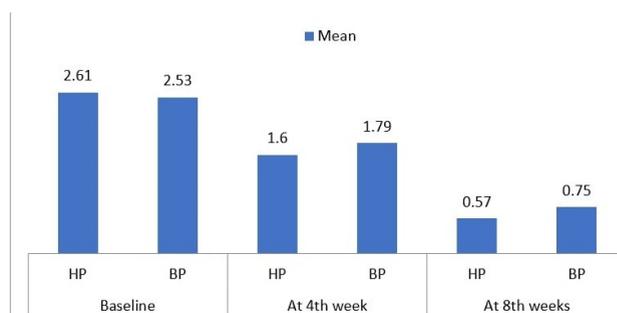


Fig. 1: Comparing inflammatory lesions at follow up with baseline

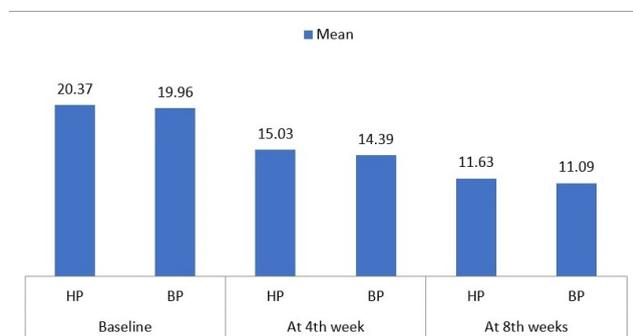


Fig. 2: Comparing non-inflammatory lesions at follow up with baseline

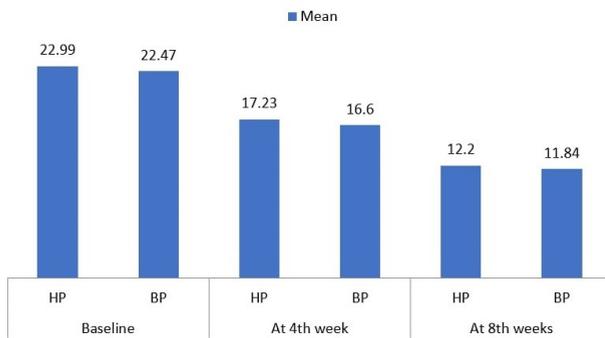


Fig. 3: Comparing total lesions at follow up with baseline

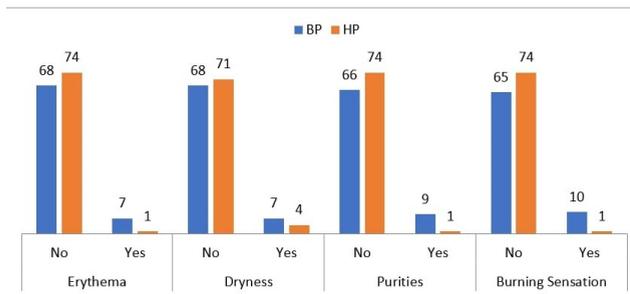


Fig. 4: Comparing tolerability of the drug

4. Discussion

Acne is the most common skin disorder of pilosebaceous unit which is characterized by excessive sebum production, redness and scaling of skin along with comedones (open and closed), papules, pustules, nodules and its sequel scarring in some patients.¹⁵

In present study we found that 1% HP was effective in mild to moderate acne. However reports have shown that products containing 3% HP have can cause local skin discoloration and are used for skin disinfection.

In present study majority of the patients were in the age group of 16-20 years (43.3%) followed by 21-25 years (26%). That means majority of the patients were of young age (<25 years). Maximum patients were female [91 (60.7%)]. In the present study, out of the 150 patients enrolled, 13 were lost to follow up, which might have been due to patients coming from peripheral areas, noncompliance with the inclusion criteria, not satisfied with the treatment and longer follow up. Majority of the patients had acne grade 2 [81 (54%)] followed by acne grade 1 [69 (46%)].

Veraldi et al evaluated the tolerability and efficacy of a novel HP-based regimen versus a BP-based regimen in 120 patients with mild to moderate acne and the inter-group comparison demonstrated that the mean Global Acne Grading System (GAGS) overall scores (combining time points) didn't differ significantly in between both the

treatments over time. ($p=0.9922$).¹⁶

In present study, maximum patients had acne on the cheek [57 (38%)] followed by Fore Head, Chin, Cheek [30 (20%)] and Neck, Chin [29 (19.3%)]. Veraldi et al studied 120 patients and found that in all patients, the face was involved and in one patient, the back was also involved.¹⁶

Comparing inflammatory lesions at follow up with baseline revealed that both the treatment were equally efficacious in reducing the inflammatory lesions at the end of 4th and 8th week ($p>0.05$). In present study non-inflammatory and total lesions at follow up revealed that both the treatment were equally efficacious in reducing the non-inflammatory lesions at the end of 4th and 8th week ($p>0.05$)

In a similar study by Kisiel et al showed that a significant reduction in acne lesions ($P=0.0003$) and number of pustular lesions ($P=0.002$) which means a trend toward reduction of number of comedones and papules was also observed among patients using HP². Muizzuddin et al¹⁷ reported that in a six-week clinical study, a 56% reduction in total number of inflammatory lesions and 45% reduction in non-inflammatory lesions.

In a recent study by Muizzuddin et al,¹⁷ published in 2013, a new HP formulation using the enzyme glucose oxidase and glucose was used. This new system was stable and the formulation was effective in reduction of number of inflammatory lesions by 68% and reduction in acne lesion size by 61% within the span of the study.

In present study comparing the tolerability of both the drugs revealed that erythema was significantly higher with BP (7 out of 8 cases) as compared to HP (1 out of 8 cases). Similarly, pruritus and burning sensation was significantly higher among the patients using BP (9 out of 10 cases) as compared to HP (10 out of 11 cases). Contrary to present study Veraldi et al compared novel HP-based regimen versus a BP-based regimen in 120 patients and found that no significant adverse events were reported or observed in either treatment arm.¹⁶

In current study assessment method was used as followed by Capizzi et al in their study, where they evaluated tolerability and the efficacy of combination therapy with HP cream and adapalene 0.1% gel and compared it with combination of BP 4% cream and adapalene 0.1% gel in treatment of AV, they reported that combination of adapalene and HP cream is an effective topical regimen in mild to moderate AV and has a better tolerability profile in comparison with the combination of BP and adapalene.

In agreement to present study Kisiel et al evaluated the safety and the anti-acne efficacy of a point-gel containing 2% H₂O₂ and salicylic acid (0.54%), phytic acid (1%), D-panthenol (1%) and vitamin PP (0.012%) and reported no skin side effects (including pruritus, skin redness or dryness).²

In present study both the treatment were equally efficacious in reducing acne ($p=0.177$) Veraldi et al evaluated the efficacy and tolerability of a novel HP-based regimen versus a BP-based regimen in 120 patients with mild to moderate acne and reported that there was no significant difference in efficacy between the two acne regimens.¹⁶ Study done by Milani et al¹⁸ who studied the role of 1% HP cream on 60 patients and reported that HP was as effective as BP in reducing both inflammatory and non-inflammatory lesions. However, 1% HP cream had a better tolerability profile.¹⁸ In a similar study by Capizzi et al¹⁹ tolerability and efficacy of 1% HP cream and 0.1% adapalene gel combination was compared with the 4% BP cream and 0.1% adapalene gel combination in 52 patients and it was reported that a significantly greater reduction in noninflammatory lesions was observed in the HP/adapalene group.

The mechanism by which HP acts is similar to the mechanism of BP.²⁰ HP reduces Propionibacterium acnes colonization.¹⁸ A theoretic future of topical HP may be represented by its use in atrophic acne scars. A report demonstrated that free oxygen radicals can stimulate as well as inhibit cultured human fibroblasts proliferation, also that fibroblasts release superoxide free radicals in concentrations that can stimulate proliferation, a finding confirmed by a dose-dependent inhibition of proliferation by free radical scavengers. Thus, providing a fast and specific trigger for fibroblast proliferation. However, sustained stimulation might result in fibrosis.²¹

A study by Fabbrocini and Panariello showed efficacy of a local applicant containing 3% HP, 1.5% salicylic acid and 4% D-panthenol in the management of mild to moderate acne vulgaris. The product was applied on the whole skin surface for 60 days and was shown to have high efficacy as compared to previous version of product containing higher HP and lower salicylic acid concentrations (4 and 0.5%, respectively).²²

In present study both the drugs had equal efficacy for both the acne grades in terms of total lesions after 8th weeks of therapy. Tolerability was similar for grade 1 acne whereas HP was more tolerable in terms of Erythema and Burning Sensation as compared to BP. Similar results were reported by the study done by Capizzi et al,¹⁹ by Milani et al¹⁸ and Veraldi et al.¹⁶ Both HP and BP are widely used for the treatment of Acne vulgaris grade 1 and 2, however there is paucity of data related to their comparison with each other in terms of their efficacy and tolerability, therefore the present study was done.

Low number of participants in each group is limitation of the study.

5. Source of Funding

None.

6. Conflict of Interest

None.

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