

The efficacy of intense pulsed light and heat energy therapy compared to benzoyl peroxide gel 2.5% in the treatment of mild and moderate acne vulgaris

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ABSTRACT

The use of technology-based light therapies such as intense pulsed light and heat energy (IPL) provides an alternative therapy for patients with acne. However, clinical evidence is required to evaluate the efficacy and safety of the IPL. This study aimed to evaluate the efficacy of IPL compared to benzoyl peroxide (BP) as standard therapies in patients with acne vulgaris. The study was conducted with randomized controlled trial parallel design involving patients with mild and moderate acne vulgaris. Acne severity was determined by the method of Combined Acne Severity Classification (CASC). Statistical analysis using repeated measurement analysis of variance was conducted to assess the reduction in lesions and number of *P. acnes* in each group followed by independent t-test to compare of both groups. A p value <0.05 was considered significant. Sixty-two patients with mild and moderate acne vulgaris were enrolled in this study and treated with IPL (32 patients) and with BP gel 2.5% (30 patients). Two patients from the IPL were dropped out. All subjects showed improvement in acne lesions. Reduction of the number of non-inflammatory lesions at IPL therapy group was not significantly different than the BP gel 2.5% at week 2 (p=0.705) and 4 (p=0.186). Reduction in the number of inflammatory lesions in the IPL treatment group was not significantly different than BP gel 2.5% at week 2 (p=0.604) but significantly higher at week 4 (p=0.003). The reduction of *P. acnes* colonization in the IPL group was significantly higher than BP gel 2.5% group at week 2 (p=0.000) and 4 (p=0.000). In conclusion, the efficacy of IPL in the reduction of the number of inflammatory lesions and the *P. acnes* colonization is better than BP on patients with acne vulgaris.

ABSTRAK

Penggunaan terapi berbasis teknologi sinar seperti intense pulsed light (IPL) dan energy panas memberikan alternative pada pasien akne. Namun demikian, diperlukan penelitian untuk mengkaji efikasi dan keamanan IPL dibandingkan dengan pengobatan standard dengan BP pada pasien acne vulgaris. Penelitian ini dilakukan dengan desain uji klinis teracak parallel terhadap pasien akne vulgaris derajat ringan dan sedang. Derajat akne diukur berdasarkan metoda *Combined Acne Severity Classification* (CASC). Analisis statistic dilakukan dengan

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analisis variansi pengukuran berulang digunakan untuk menilai penurunan jumlah lesi dan jumlah *P. acnes* pada tiap kelompok dilanjutkan dengan uji-t untuk membandingkan kedua kelompok. Nilai $p < 0,05$ digunakan untuk menyatakan perbedaan secara bermakna. Enam puluh dua pasien subyek dengan tipe kulit IV dan V diikuti dalam penelitian ini dan 32 pasien mendapatkan terapi IPL dan 30 pasien mendapat gel BP 2,5 %. Dua pasien kelompok IPK keluar dari penelitian karena efek samping. Hasil penelitian menunjukkan semua subyek mengalami perbaikan lesi akne. Penurunan jumlah lesi non-inflamasi pada kelompok IPL tidak berbeda bermakna dengan kelompok BP 2,5 % pada minggu ke 2 ($p = 0,705$) dan ke 4 ($p = 0,186$). Jumlah lesi inflamasi kelompok IPL tidak berbeda pada minggu ke 2 ($p = 0,604$) tetapi lebih baik pada minggu ke 4 dibandingkan kelompok BP ($p = 0,003$). Penurunan jumlah koloni *P. acnes* menunjukkan perbaikan nyata pada kelompok IPL dibanding kelompok BP baik pada minggu ke 2 ($p = 0,00$) maupun minggu ke 4 ($p = 0,00$). Disimpulkan, efikasi IPL dalam menurunkan jumlah lesi inflamasi dan koloni *P. acnes* lebih baik dibandingkan BP pada pasien dengan acne vulgaris.

Keywords: acne vulgaris – *P. acnes* – blackhead -intense pulsed light and heat energy - benzoyl peroxide -

INTRODUCTION

Acne vulgaris is a common skin disease that affects almost all teenagers and adult population.^{1,2} In outpatients clinic of the Division of Cosmetic, Department of Dermatology and Venereology Dr. Sardjito General Hospital Yogyakarta, acne vulgaris is one of the three major diseases that are often found with a prevalence of approximately 71% of total visits during the period of 2006-2011. The prevalence of acne vulgaris in Hong Kong amounted to 91.3%, with ages ranging from 15-25 years and 26.6% of respondents suffered from psychological disorders.³ Psychological effects caused by acne induce the loss of self-esteem and depression which affect their quality of life.^{4,5} The negative effects of acne need to be anticipated by providing education, as well as the effective and efficient acne treatment.⁶

Various modalities for acne therapy are available.⁷ The involvement of various factors related to the pathogenesis of acne vulgaris leads to the emergence of variety of acne therapy modalities.⁸⁻¹⁰ Factors involved include follicular epidermal

hyperproliferation, increased production of excessive sebum, Propioni bacterium acnes hypercolonization and inflammatory.¹¹ Moreover, it is also needed to consider other factors, such as the duration of disease, response to prior therapy, predisposing to post-inflammatory scars and hyperpigmentation. Patients preference and cost of acne treatment regimens should also be considered to treat acne. . In addition, the late onset of therapeutic action often leads to patients' non-compliance in running acne therapy.^{12,13} Another problem is the resistance of *P.acnes* due to long-term use of antibiotics that may cause refractory to therapy and the increasing rate of disease recurrency.^{13,14}

Benzoylperoxide (BP) is one of the standard therapy of mild and moderate acne that is widely used with a concentration of 2.5% to 10% with the goal of reducing *P. acnes*.¹⁵ Therapeutic effectiveness is equivalent between BP gel 2.5%, 5% and 10%. The irritation effect may be lower by using the concentration of BP gel 2.5%.¹⁶ Moreover, benzoyl peroxide can also reduce the potential of *P. acnes* resistance to antibiotic.¹⁷⁻¹⁹

Utilization-based light therapy technology either as mono therapy or in combination with standard therapy provides an alternative treatment option for acne patients.^{13,20} Light therapy target is *P. acnes* or damage to the pilosebaceous unit.²¹ Intense pulsed light technology (IPL) as a light-based therapy was developed as an alternative therapy for acne because of its efficacy in accelerating the photochemical reaction of porphyrin, faster onset of action and ability to reduce the risk of bacteria resistance.²² IPL technology was developed and combined with thermal energy, known as pulsed intense light and heat energy based on thermal shock mechanism.¹¹

Research on the effectiveness of the IPL treatment for acne vulgaris has been conducted in many countries with various results.⁷ Based on the results of systematic review by Hamilton et al.²¹ clinical trials with light therapy has been done with several methods; i.e. comparing with placebo as a control, topical therapy as a control, comparing light therapy with different wavelength, or combined with microdermabrasion as a control. According to identification of the review, they obtained 3 clinical trials on the comparative use of light therapy with topical therapy as a control. The Global Alliance to Improve Outcomes in Acne Group stated that the existing research, in particular light therapy, has varying qualities, but it still rare that light-based therapy is compared with validated pharmacological therapy.²³ Currently, there is not enough clinical data to support the recommendation of using light-based system therapy²⁴, that it still needs more evidence-based research to explain the clinical efficacy and safety of light therapy with different degrees of acne as well as a greater number of subjects and longer follow-up period.²⁵ To date, no reported comparative

data on the effectiveness of intense pulsed light heat energy therapy with BP gel 2.5% for mild and moderate acne vulgaris.

MATERIALS AND METHODS

This study was a randomized controlled trials with parallel design. Subjects were patients with mild and moderate acne vulgaris, had a skin type IV and V. Sample was determined by consecutive sampling. Acne severity was determined by the method of combined acne severity classification (CASC). The study was done in October 2012-January 2013. Patients had provided informed consent and agreed not to change their skin care during this trial. All patients in IPL group were instructed to come to the study twice weekly for 4 weeks and those in BP 2.5% group were instructed to apply the topical twice daily after washing the facial skin. The condition of acne and side-effects were monitored before and at week 2 and 4.

The independent variables were the treatment using intense pulsed light and heat energy (IPL) and topical benzoyl peroxide gel 2.5% (BP 2.5%). Dependent variable was the result of the effectiveness of such therapy as assessed by a reduction in non-inflammatory and inflammatory lesion count number, and decrease number of *P. acnes*. Statistical analysis using repeated measurement analysis of variance to assess the reduction in lesions and *P. acnes* in each group. Comparison of the difference in the mean reduction in lesion and *P. acnes* between the two treatment groups were statistically analyzed by independent t-test with a significance value of $p < 0.05$.

The study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta.

RESULTS

A total of 62 patients with mild and moderate acne vulgaris with skin types IV and V were enrolled in this study and then randomized into two groups. Thirty-two patients included in the test group received the IPL, 30 patients were included in the

control group and treated with BP gel 2.5%. Two patients from the IPL otherwise dropped out due to could not meet the requirements to come routinely to the study. Comparison of characteristics of subjects between two groups is presented in TABLE 1. There was no significant difference between the two groups ($p > 0.05$).

TABLE 1. Baseline demographic and clinical characteristics of subjects

Subjects	IPL(n = 30)	BP 2.5% (n = 30)	p
Age (mean ± SD)	21.7±3.08	21.27 ±2.72	0.893
Sex			
• Male	17 (56.7%)	19 (63.3%)	0.598
• Female	13 (43.3%)	11 (36.7%)	
Skin type			
• Skin type IV	17 (56.7%)	14 (46.7%)	0.438
• Skin type V	13 (43.3%)	16 (53.3%)	
Acne severity			
• Mild	15 (50%)	14 (46.7%)	0.796
• Moderate	15 (50%)	16 (53.3%)	
Count the number of lesions			
• Non-inflammatory	42.01 ± 13.51	39.80 ± 14.79	0.622
• Inflammatory	18.40 ± 5.17	18.23 ± 6.90	0.133
<i>P. acnes</i> colonization (mean ± SD)	1787.23 ± 481.25	1610.20 ± 447.06	0.485

In each study group, the mean non-inflammatory, inflammatory lesions and the number of *P. acnes* were significantly decreased. FIGURE 1 shows the significantly decrease in the average number of non-inflammatory lesions after 2 weeks and 4 weeks of treatment ($p < 0.05$). The mean percentage reduction in non-inflammatory lesions in

the IPL group based on the observations of week 2 and week 4 of treatment were 31.8% ($p = 0.000$) and 85.69% ($p = 0.000$) respectively, while in BP 2.5% group, the mean percentage reduction in non-inflammatory lesions according to the observation of week 2 and week 4 of treatment were 30.56% ($p = 0.000$) and 42.44% ($p = 0.000$) respectively.

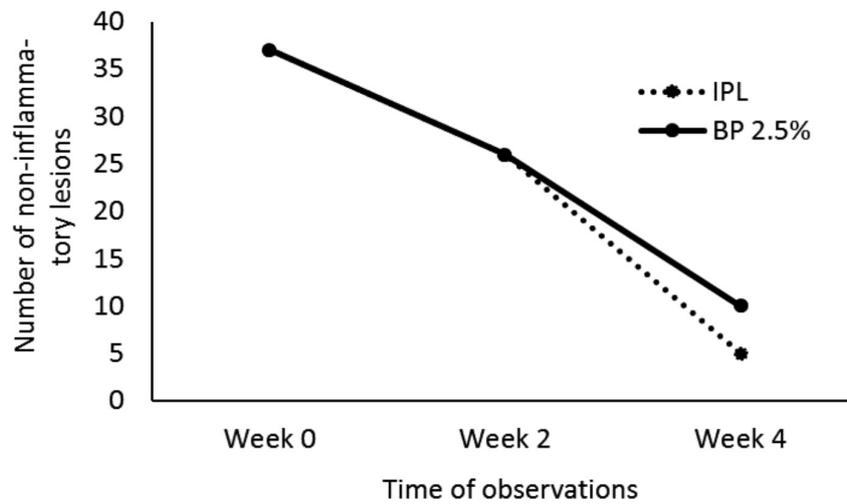


FIGURE 1. Comparison of mean decline in the number of non-inflammatory lesions in both study groups

The mean number of inflammatory lesions in both study groups showed a significantly different ($p < 0.05$) after 2 weeks and 4 weeks of treatment (FIGURE 2). In the IPL group, the mean percentage reduction in inflammatory lesions based on the observations of week 2 and week 4 compared to week 0 were

48.47% ($p = 0.000$) and 85.02% ($p = 0.000$) respectively. In BP 2.5% group, the mean percentage reduction in inflammatory lesions based on the observation of week 2 and week 4 compared to week 0 were 41.17% ($p = 0.000$) and 69.65% ($p = 0.000$) respectively.

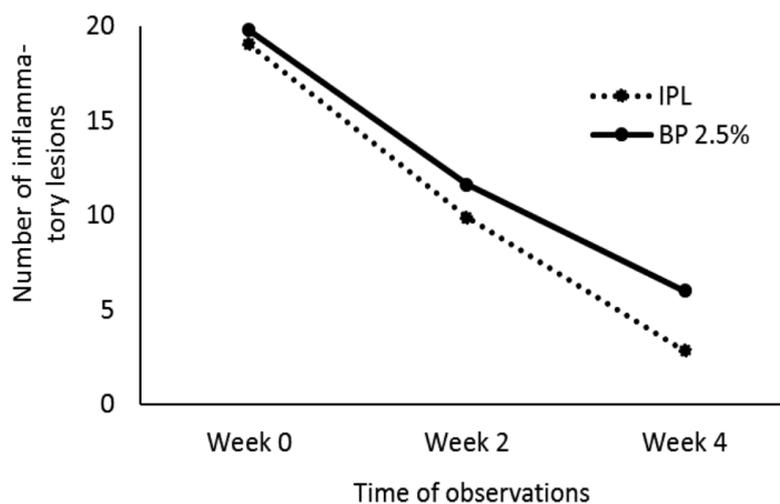


FIGURE 2. Comparison of mean decline in the number of inflammatory lesions in both study groups

The mean colonization of *P. acnes* showed reduction in both groups. However, IPL group showed more significant reduction ($p=0.000$)

based on the observation week 0, 2 and 4 compared to week 0, as shown in FIGURE 3.

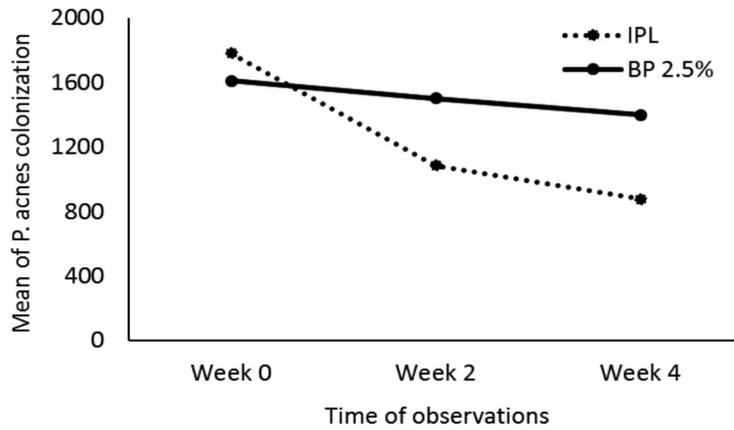


FIGURE 3. Comparison of mean reduction of *P. acnes* colonization in both study groups

The IPL therapy improved reduction of *P. acnes* higher than BP 2.5% group. Mean percentage of *P. acnes* reduction in IPL group showed 39% ($p=0.000$) after 2 weeks of treatment and 50.78% ($p=0.000$) after 4 weeks of treatment. BP 2.5% group showed that reduction of *P. acnes* after 2 weeks and 4 weeks of treatment were 6.8% ($p=0.000$) and 13.19% ($p=0.000$) respectively.

The treatment efficacy was determined by the percentage of reduction of non-inflammatory lesions, inflammatory lesions and the number of *P. acnes* on the observation of week 2 and week 4 compared to week 0 between the two groups. There was no significantly difference between non-inflammatory lesions at week 2 ($p=0.705$) and week 4 ($p=0.186$) of treatment in both groups (FIGURE 4).

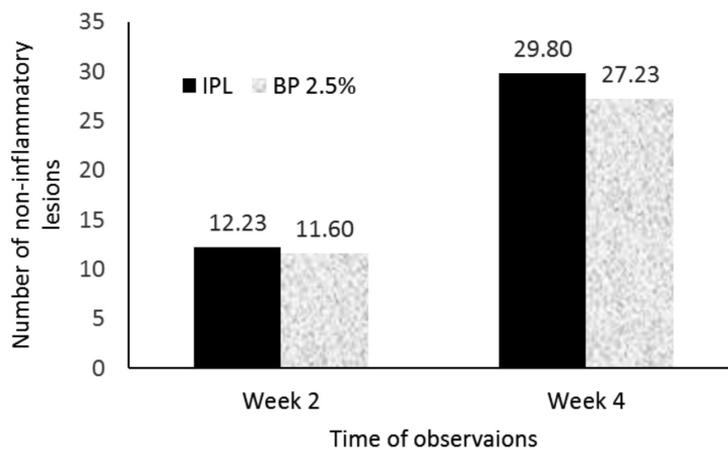


FIGURE 4. Comparison of difference in number of non-inflammatory lesions in both groups

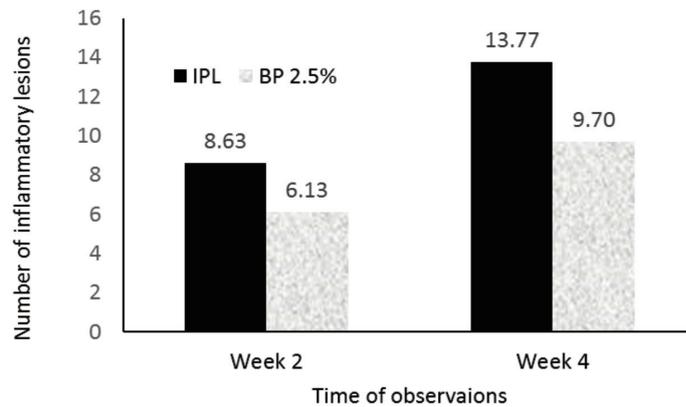


FIGURE 5. Comparison of difference in number of inflammatory lesions in both groups

According to the comparison of mean difference in the number of inflammatory lesions, it was found that the IPL was more effective in reducing inflammatory lesions at week 4 compared to BP 2.5% ($p=0.003$).

The effectiveness of these two therapies in inflammatory lesions observation on week 2 was not significantly different ($p=0.604$), as shown in FIGURE 5.

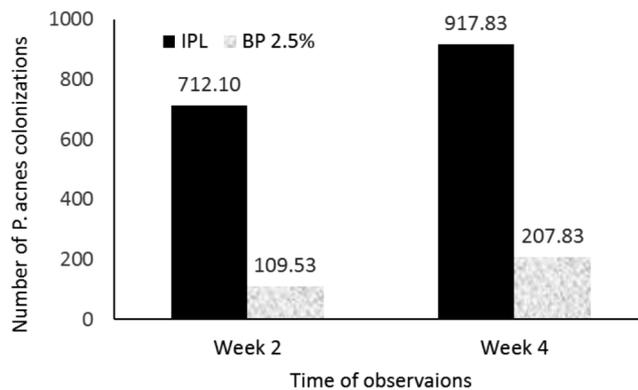


FIGURE 6. Comparison of difference in P. acnes colonization

Based on the treatment efficacy by comparing the mean difference in the number of P. acnes on the evaluation of 2 weeks and 4 weeks of treatment, it was found that the IPL was more effective in reducing the colonies of P. acnes compared with BP 2.5% therapy ($p=0.000$), as shown in FIGURE 6.

Based on the subjects assessment of therapeutic results observed between the two groups at 4 weeks of treatment, no significantly different was found ($p=0.188$), as shown in TABLE 2.

TABLE 2. Subjects assessment of IPL and BP 2.5% groups at week 4

Subjects assessment	IPL (n=30)	BP 2.5% (n=30)
Getting worse	0	0
No improvement	0	0
Mild improvement	1 (3.33%)	3 (10%)
Moderate improvement	3 (10%)	5 (16.67%)
Overall improvement	26 (86.67%)	22 (73.33%)

All the subjects were monitored for the side effects of therapy. Mild erythema was earned by 2 patients (6.67%) in IPL therapy, while dry skin was earned by 4 patients

(13.3%) in BP 2.5% therapy. In the subjects assessment of side effects in both groups, there was no statistically significant difference (p=0.334) as shown in TABLE 3.

TABLE 3. Side effects in IPL dan BP 2.5% groups

Side effects	IPL (n=30)	BP 2.5% (n=30)
Mild erythema	2 (6.67%)	0
Dry skin	0	4 (13.33%)
No side effects	28 (93.33%)	26 (86.67%)

DISCUSSION

Acne vulgaris is known not only as a follicular infection but also as a chronic inflammatory disease of the pilosebaceous unit. Pathogenesis of acne includes increased sebum production, hypercolonization of *P. acnes*, follicular hyperkeratinization and release of inflammatory mediators. *Propionibacterium acnes* stimulates T cells, macrophages and keratinocytes to produce inflammatory cytokines through innate and acquired immunity.²⁶ By considering factors involved in the pathogenesis of acne, a variety of treatment options has emerged.

This study was conducted to compare the efficacy and safety of two different kinds of therapy, intense pulsed light and heat energy therapy and BP gel 2.5%, during the period of 4 weeks in patients with mild and moderat acne vulgaris. The effectiveness of BP¹⁵ and IPL⁷ therapies in mild and moderate

acne has been studied in numerous researches with varying results, but only few studies have compared the two kinds of therapy directly.²³ In this study, the comparison of treatments of acne with intense pulsed light and heat energy and BP gel 2.5% demonstrated an effective result for acne treatment on non-inflammatory and inflammatory lesions. In this study, the efficacy of the therapy based on the assessment of mean reduction in non-inflammatory lesions, inflammatory lesions and colonization of *P. acnes* were assessed at week 0, 2 and 4. Moreover, subjects assessment of treatment outcomes and its side effects were also observed. In the assessment of week 2 and 4, the IPL showed that mean improvement of non-inflammatory lesions decreased by 85.69% and inflammatory lesions by 85.02% whereas, in BP 2.5% group, the mean reduction in non-inflammatory lesions and inflammatory lesions were 42.44% and 69.65% respectively. The

results of this study was slightly higher than the study by Papageorgiou *et al.* (2000) with improved non-inflammatory lesions of 75% and inflammatory lesions of 60%.

Benzoyl peroxide is a potent antimicrobial agent, because of its lipophilic ability that enables BP to penetrate into the pilosebaceous duct and has proven its efficacy in superficial inflammatory lesions. When applied to the skin, BP decomposes in order to release oxygen free radicals, which has a strong bactericidal activity of sebaceous follicles as well as an anti-inflammatory agent. Benzoyl peroxide has an effect on non-inflammatory lesions by reducing follicular hyperkeratosis.^{7,27} Treatment of acne with both IPL and BP has the same target in the pathogenesis of acne, such as *P. acnes*, sebaceous follicles and inflammation. Technology intense pulsed light (IPL) was developed as an alternative therapy for acne because of its efficacy in accelerating the photochemical reaction of porphyrin, faster onset of action and ability to reduce the risk of bacterial resistance.²² The IPL technology was developed and combined with thermal energy, known as intense pulsed light and heat energy based on the thermal shock mechanism.¹¹ Overall, the provision of therapy in both groups were equally able to reduce colonization of *P. acnes*, and in this study, IPL therapy was able to reduce the colonization of *P. acnes* higher (50.78%) compared to BP 2.5% treatment (13.19%). In this study, the colonization of *P. acnes* was determined by fluorescence follicular red-orange that is directly proportional to the levels of sebum, which is in accordance with the study of Dobrev²⁸ which states that the porphyrin will appear as a point of red-orange fluorescence in the follicle, which indicates the presence of *P. acnes* bacteria that live in or on the surface of

the decline in the number of follicles. The reduction of *P. acnes* accompanied by reduction of porphyrin concentrations will lead to the clinical improvement. Therefore, the determination of porphyrin fluorescence can assist in the evaluation of the degree of acne severity.²⁹

The efficacy of therapy was investigated by comparing the mean number of non-inflammatory lesions and inflammatory lesions at 2 and 4 weeks of treatment compared with the baseline values. This study demonstrated effective results at 4 weeks of treatment on the inflammatory lesions ($p < 0.05$) and was not effective on non-inflammatory lesions. Hamilton *et al.*²¹ stated that light-based therapy would provide improved lesion especially in inflammatory lesions such as papules and pustul, while non-inflammatory lesions such as comedo and cysts are generally resistant to therapy. This result indicates that decreased colonization of *P. acnes* was higher in IPL compared to BP 2.5%, both on the evaluation of week 2 and week 4 of treatment ($p < 0.05$). This result is suitable with the theory that *P. acnes* produce porphyrins as part of its normal life cycle. When porphyrins are exposed to visible light or IPL, then the chemistry will be activated, leading to induce a photodynamic reaction that causes destruction of *P. acnes* and sebaceous gland.³⁰ Benzoyl peroxide showed its bactericidal activity through oxidation, causing the release of reactive oxygen that will oxidize a high-protein on the cell membrane of bacteria resulting in the destruction of *P. acnes*.³¹ The results of this study indicate that the destruction of *P. acnes* with photodynamic reaction is more effective than oxidation by benzoyl peroxide.

Side effects from the use of benzoyl peroxide may lead to irritation and dryness of skin.³⁰ In this study, there were 4 (13.3%)

subjects who complained about the dryness of skin. Side effects that occurred in the use of IPL was generally relatively minimal. By modifying the parameter variations in therapy including the outgoing energy, pulse duration and pulse delay, it is possible to minimize the severity of side effects.³¹ Mild erythema was observed on 2 (6.67%) subjects in the IPL group. Otherwise, there was no significant difference in the two groups. Comparison of price therapy for IPL was higher than BP 2.5%. It can be concluded that there was no significant difference between the IPL and the BP 2.5% groups according to the subjects assessment of therapeutic results ($p>0.05$). Overall, all patients of the two groups were satisfied with the results of therapy.

CONCLUSION

In conclusion, the efficacy of IPL in the reduction of the number of inflammatory lesions and the *P. acnes* colonization is better than BP on patients with acne vulgaris, therefore the IPL can be used as standard therapy of acne vulgaris.

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