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Comparison Of Effectiveness And Duration Of Recovery Of Acne Vulgaris Treatment Using A Topical, Topical Plus Systemic, And Topical Plus Laser

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ABSTRACT

Background: Acne vulgaris is a common skin condition mainly affecting those in puberty and young adults. Conventional treatments like topical and systemic medications have limitations such as high discontinuation rates due to side effects, poor response or delayed therapeutic effect. Laser treatment can be used as an alternative treatment.

Objective: This study compared the treatment effectiveness and recovery duration between topical, topical plus systemic, and topical plus laser in treating acne vulgaris.

Material and Method: Ninety patients with a diagnosis of acne vulgaris who received treatment at Erha Dermatologi private clinics in Medan and Jakarta were followed up prospectively for 12 weeks. Patients were divided into three treatment groups (topical only, topical plus systemic, and topical plus laser) of their choice. Treatment efficacy was compared based on the number of lesions, IGA, and recovery time, and was measured at baseline, 2 weeks, 4 weeks, 8 weeks, and 12 weeks of treatment.

Results: All treatment modalities resulted in significant improvement in acne lesions at the end of 3 months. However, the topical plus laser group had faster and more significant improvement compared to topical and topical plus systemic, with p-value < 0.01.

Conclusion: All therapies were effective at 12 weeks, but the combination of topical plus laser treatment showed the fastest and most consistent improvement from week 4, with the potential for long-term cost-effectiveness.

Keywords: Acne treatment: topical, systemic, laser therapy, lesion count, IGA.

INTRODUCTION

Acne vulgaris is one of the commonest chronic skin disease involving the pilosebaceous glands particularly at the face and trunk, manifested as open and closed comedones, papules, and pustules (Vasam et al., 2023). On top of this, patient with severe acne vulgaris also develop nodules and cysts, increasing the risk permanent acne scar (Vasam et al., 2023). The prevalence varies accross different countries depending on the age group and ethnicity of the patients studied, as well as the diagnostic methods used in the study. Overall, acne affects 26.8% of young adults to nearly 96% of teenagers (Heng & Chew, 2020).

Many regarded acne vulgaris as a benign dermatological disease as it did not lead to mortality and serious morbidity. Nevertheless, untreated, it can cause significant physical and psychological complications to the patients particularly for those who develop scarring and suffers from severe acne. This disease should not be taken lightly as literatures have shown that acne especially in the severe spectrum is associated with serious psychological disturbance like stress and depression and can significantly impaired the social function and quality of life of the sufferer (Chuah & Goh, 2015; Morshed et al., 2023; Ollyvia et al., 2021; Tayel et al., 2020). Furthermore, patient with severe or nodulocystic acne have higher risk of experiencing suicidal thoughts, especially in women, and should be treated aggresively with treatment modality which offer faster resolution of lesion (Halvorsen et al., 2011). Thus, timely detection and effective intervention that could treat the acne lesion faster are crucial in avoiding these complications, and improving overall patients' quality of life.

Currently available treatment of acne vulgaris mainly involved topical treatment and systemic treatment. For mild acne, the prefered treatment is topical therapies whether monotherapy or as combinations such as benzoyl peroxide, topical antibiotics, salicylic acid, topical antibiotic, azelaic acid, and topical retinoids like adapalene, tazarotene, and tretinoin (Malaysian Health Technology Assessment Section (MaHTAS), 2022; Sjarif M. Wasitaatmadja et al., 2016). Nevertheless, this type of treatment require a prolonged period of usage and compliance to exhibit its therapeutic effect, typically six to twelve weeks of continuous usage which is not favoured for certain group of patients, especially for those who is keen to obtain quick recovery (Sevimli Dikicier, 2019). Besides, it is also commonly associated with local side effects that can lead to premature discontinuation of therapy like skin irritation and redness, which commonly occurs especially in the early stages of use (Lam Hoai et al., 2021; Sevimli Dikicier, 2019).

Patients with moderate to severe acne, not tolerating the topical medication, or shows unsatisfactory response to the topical medication might require systemic medication for their acne treatment. The medications include oral antibiotics, oral isotretinoin, as well as hormonal therapy. The oral antibiotics and hormonal medication usually combined with the topical medication, whereas oral isotretinoin is usually be used as monotherapy. Oral isotretinoin is regarded as the most potent acne medication and effectively targets all mechanisms contributing to acne, such as reducing sebum production, altering abnormal follicular keratinisation, inhibiting Propionibacterium acnes colonisation and posing anti-inflammatory effects (Vasam et al., 2023). It is indicated for patient with acne-induced scarring, severe nodulocystic acne, and unsatisfactory responses toward two topical agents plus antibiotics or hormonal therapies (Malaysian Health Technology Assessment Section (MaHTAS), 2022). However, there were few issues pertaining to the systemic medications. Although isotretinoin is highly potent, this medication also could lead to serious side effects necessitating close monitoring and screening. It could alter the mood, lead to skin dryness and alopecia, dry eye, elevate the liver enzyme, increasing the level of cholesterol, and cannot be used in pregnant or women who plan for pregnancy due to its potential

teratogenicity (Kapała et al., 2022). Whereas, long term use of topical and oral antibiotic could lead to bacterial resistance and ineffective treatment (Legiawati et al., 2023). Given the limitation of the topical and systemic treatments, there is a need to find effective strategy to treat acne patients especially for those who are unable to adhere to the existing medication or tolerate it's side effects, as well as patient who is keen to have faster healing.

Light and laser treatment has emerged as a promising alternatives to the current therapy in treating acne vulgaris. The examples of these treatment includes blue and red light as well as laser such as c-1064 nm Long-Pulsed Neodymium: Yttrium-Aluminium-Garnet Laser (Nd: YAG), c-intense pulsed light laser, and so on. The ways it treats acne are mainly by reducing Propionibacterium acnes proliferation and regulating sebaceous gland function (Moftah & Moftah, 2022). Existing data have shown that this treatment modality resulted in a quick improvement of acne lesion, offering shorter recovery time, and has minimal side effect (Olugbade et al., 2025). Plus, laser treatment is also more convenient as it require less frequent treatment session and the need of strict adherence for topical and systemic treatment, making it an ideal solution for managing acne vulgaris for specific population.

Despite the availability of data on the effectiveness of laser treatment for acne vulgaris, there is scarcity of data on the cost-effectiveness of this kind of treatment modalities given the higher upfront cost of this treatment compared to conventional treament. There is also no comparative study to evaluate the effectiveness of conventional acne treatment versus laser treatment. Even though the treatment cost of conventional medication is accessible by most patients, the improvement of acne lesion could take several weeks to months to improve. Conversely, laser treatment provides expedited improvement in reducing acne lesion. Although the upfront treatment cost is higher, the overall cost of this treatment modality could be offset by its more rapid recovery time and lower financial impact resulted from fewer clinic visit and lower travel costs as well as and fewer lost workdays.

The aimed of this study was to compare the efficacy of topical, topical plus systemic, and topical plus laser treatment in terms of reduction of acne lesion and also the difference of recovery days.

MATERIAL AND METHODS

Study design and subjects

This study was conducted through a prospective convenience sampling method measuring the outcomes of different acne treatment regime between four different private clinics at Medan, Indonesia. Each clinic was assigned to one of the treatment regime tested in this study to minimise contamination. The clinics were Erha Dermatology Clinic in Medan for topical treatments, Erha Pondok Indah Clinic in Jakarta for topical plus systemic treatments, and Gandaria Clinic and Deli Park Clinic in Medan for topical plus laser treatments. All acne vulgaris patients who came to these four clinics for treatment were screened for inclusion and exclusion criteria. Patients with inclusion criteria and did not have exclusion criteria and were able to follow the treatment and research protocol, were invited for recruitment for the study.

As these clinics were private clinics, the patients usually chose their preferred treatment after being thoroughly examined and briefed about the treatment options. Thus, no randomisation was performed throughout the study. Instead, this study utilised a prospective cohort study design whereby the treatment regime chosen by the patient and the outcome were assessed at each of the specific study periods.

The inclusion criteria were male and female patients aged 16 years and above with mild to severe acne and capable to follow with the treatment and research protocol. Patients were excluded if they were pregnant and breastfeeding, had received previous acne treatment within 3 months, received oral isotretinoin within the last 1 year, received antibiotic treatment in the last month, had received laser treatment for acne, history of photosensitivity, had a tendency to develop keloid or hypertrophic scars, and also had history of liver disease.

The data was collected from April 2024 until August 2024, where 30 patients were recruited for each treatment arm using consecutive convenience sampling method. All subjects with inclusion criteria and did not have exclusion criteria were recruited until the required number of subjects was met. Following thorough history taking and physical examination, the patients then were briefed about the treatment options, and subsequently, chose their preferred treatment regimen. All subjects were closely followed-up and had continued their treatment regimen from the beginning until the end.

Treatment protocol

Topical medications used in this study were mostly combined topical medication and as listed in table 1, and the systemic medications used in this study were as listed in table 2. In this study, all topical medications and systemic medications were grouped as a topical group and systemic group as a whole.

Patients who were treated with topical treatment received any of the topical medication, while patients who were treated with topical plus systemic treatment received any of the topical medications plus one of the systemic medications, and patients who were treated with topical plus laser treatment also received any of the topical medications plus the laser treatment. The choice of the medication and treatment used was based on the recommendation by the treating doctor after thorough clinical evaluation.

No	Topical medication
1	Azelaic acid + clindamycin + ceramide
2	Clindamycin + nicotinamide
3	Clindamycin + Flacinol Acide + Ceramide
4	Clindamycin + benzoyl peroxide + Azelaic acid
5	Azelaic Acid + Clindamycin + Benzoyl Peroxide
6	Azelaic Acid + Niacinamide + adapalene
7	Adapalene + benzoyl peroxide + nicotinamide
8	Azelaic Acid + nicotinamide
9	Azelaic Acid + Niacinamide + Tranexamic

Table 1. Topical medications used in the study.

Patients who used topical medications were instructed to wash their face with a mild cleanser and dry it using a clean towel. The topical medication is then applied thinly to the acne lesion area but not near to the eyes, lips, and mucous membranes. These medications must be applied daily at night to minimise the risk of irritation, and subsequently the frequency was increased to twice daily, morning and evening, after 2 weeks if they can tolerate it. Besides, they were also advised to apply sunscreen with minimum sun protection factor (SPF) of 30 in the morning to avoid sunburn and to use moisturiser if they develop skin dryness. They were told to inform the treating doctor if they develop skin irritation, redness or peeling.

No	Systemic medications
1	Cefixime
2	Clindamycin
3	Cefditoren
4	Doxycycline
5	Pivoxil Zincore Erha

Table 2. Systemic medications used in this study.

The systemic antibiotic was prescribed according to the acne severity and the patient's medical history, with the treatment duration limited to 12 weeks. Besides, the Zincore was added to enhance skin healing and to reduce the inflammation.

The laser used in this study was the 1064 nm Long-Pulsed Neodymium: Yttrium-Aluminum- Garnet Laser (Nd: YAG). Patients who were treated with laser received laser treatment at the first (0 week) and second visit (2 week) within the 2 weeks interval. They were also received topical medication from the beginning up to 12 weeks.

For the laser treatment preparation, the patient’s face was washed with water, followed by application of anaesthetic creams (lidocaine 2.5% and prilocaine 2.5%) and left for around 40 minutes. The skin then was cleaned with 70% alcohol. The acne lesion area then was treated with three overlapping passes consecutively, while the perilesional area which covers around 2 cm fromt the lesion and the clear area around 10 cm from the lesion were treated with single pass. The fluency used was 35 J/cm2 for the acne lesion and 30 J/cm2 for the adjacent unaffected tissue. The pulse frequency used was 20 ms, the point size was 10 mm, and the cooling tip temperature was 4^{o} C.

Evaluation

The patients' faces were evaluated using IGA to classify their acne severity into mild, moderate, and severe and their lesions were counted at baseline visit and at 2, 4, 8, and 12 weeks of treatment. All treatment modalities were started at the baseline visit itself. Then, the IGA score and acne lesions were recorded for each treatment group to determine which treatment regime had most significant improvement.

Tool Data analysis:

IGA scale data was tested for normality using the SPSS application. The test results showed that the IGA data were not normally distributed ($p > 0.01$), thus ANOVA test could not be performed. Therefore, the non-parametric test specifically Kruskal-Wallis was utilised to determine the significance of each variable.

RESULT

A total of 90 patients participated in this study, with 30 patients for each topical, topical plus systemic, and topical plus laser treatment group. The sociodemographic profile is as table 3.

Characteristic	Topical		Systemic		Laser		p-value
	n	%	n	%	n	%	
AGE							
16 to 28	20	66.7	20	66.7	20	66.7	0.876
29 to 38	8	26.7	6	20.0	6	20.0	
39 to 48	2	6.7	4	13.3	4	13.3	
Total	**30**	**100.0**	**30**	**100.0**	**30**	**100.0**	
Gender							
Male	0	0.0	10	33.3	3	10.0	0.001
Female	30	100.0	20	66.7	27	90.0	
Total	**30**	**100.0**	**30**	**100.0**	**30**	**100.0**	
Education							
High School	1	3.3	5	16.7	7	23.3	0.003
Diploma	3	10.0	9	30.0	12	40.0	
Bachelor's degree	26	86.7	16	53.3	11	36.7	
Master	0	0.0	0	0.0	0	0.0	
PhD	0	0.0	0	0.0	0	0.0	
Total	**30**	**100.0**	**30**	**100.0**	**30**	**100.0**	
Occupation							
Government	0	0.0	8	26.7	7	23.3	0.007
Student	1	3.3	5	56.7	19	63.3	
Self-employed	29	96.7	17	16.7	4	13.3	
Pensioner	0	0.0	0	0.0	0	0.0	
Not working	0	0.0	0	0.0	0	0.0	
Total	**30**	**100.0**	**30**	**100.0**	**30**	**100.0**	
Salary							
<123.68 USD	1	3.3	1	3.3	0	0.0	0.000
>123.68 USD <309.21 USD	15	50.0	5	16.7	27	90.0	
>309.21 USD	14	46.7	24	80.0	3	10.0	
Total	**30**	**100.0**	**30**	**100.0**	**30**	**100.0**	
Marital status							
Married	14	46.7	15	50.0	11	36.7	0.557
Not married	16	53.3	15	50.0	19	63.3	
Total	**30**	**100.0**	**30**	**100.0**	**30**	**100.0**	

Table 3 Socio-demographic characteristics of patients.

The 16 to 28 years old age group dominated all treatment modalities, representing 66.7% of patients in the topical therapy, topical plus systemic, and topical plus laser groups. Meanwhile, the 29 to 38 and 39 to 48 age groups showed a gradual increase in preference for more advanced treatments, particularly topical plus systemic and topical plus laser therapies. Interestingly, the systemic and laser groups had

identical age distributions, suggesting a stable trend without notable variation across these two modalities. However, the observed differences in age distribution were not statistically significant (p = 0.876), indicating age was not a determining factor in the treatment selection. In contrast, gender distribution varied significantly across the treatment groups. All patients in the topical-only group were female (100%), while the topical plus systemic group consisted of 33.3% males and 66.7% females. The topical plus laser group had a lower proportion of male participants (10%) compared to females (90%). This variation was statistically significant with the p-value of 0.001 suggesting a strong association between gender and treatment choice. The data imply that female patients were more inclined toward topical therapies, especially the more advanced laser-based treatments, compared to their male counterparts.

Lesion count

Table 4 illustrates the efficacy of topical, topical plus systemic, and topical plus laser treatment over a 12-week period by tracking changes in acne lesion counts. All groups showed a steady and significant reduction in lesion count at each time point, confirmed by the Kruskal–Wallis test with a p-value < 0.05. The topical plus laser group demonstrated the most dramatic improvement, reducing the mean lesion count from 21.17 at baseline to just 0.10 by week 12. This was followed by the topical plus systemic group, which decreased from 15.50 to 0.17, while the topical-only group reduced from 15.17 to 0.40. These findings suggest that while all treatments were effective, the combination of topical plus laser therapy provided the most rapid and consistent results in reducing acne lesions.

No	Treatment	Lesion count					Sig.
		baseline	2–weeks	4–weeks	8-weeks	12–weeks	
		Mean	Mean	Mean	Mean	Mean	
1	Topical	15.17	11.83	8.13	4.10	0.40	0.000
2	Systemic + Topical	15.50	12.03	7.87	2.40	0.17	0.000
3	Laser + Topical	21.17	11.40	3.40	1.13	0.10	0.000

Table 4. Lesion count of topical, topical plus systemic, and topical plus laser

IGA Score

Table 5 shows the changes in IGA scores of each treatment group from baseline up to 12 weeks, highlighting differences in the rate of acne severity reduction and consistency of outcomes among the three groups. At baseline, most patients in the topical group (73.3%) presented with mild acne, while 23.3% had moderate severity. In contrast, 90% of patients in the topical plus systemic group exhibited moderate acne, and 76.7% of those in the topical plus laser group had severe acne. These baseline

differences indicate that the laser group began with the most severe acne, yet still demonstrated remarkable progress throughout the treatment period.

After two weeks of treatment, all groups showed significant clinical improvement, with the majority of patients showing mild acne severity. In the topical group (93.3%) and in the topical plus systemic group (96.7%), and 66.7% in the topical plus laser group, there was a rapid initial improvement. By week 4, all patients in the laser group had achieved clear skin, while the majority of patients in the topical and topical plus systemic groups remained in the "virtually unchanged" or mild category (80% and 66.7%, respectively).

At week 8, the results achieved by the laser plus topical group remained consistent, maintaining clear skin. In comparison, the systemic plus topical group showed further improvement, with 33.3% of patients achieving clear skin and 63.3% still showing minimal acne. The topical-only group showed slower progress, with only 10% achieving clear skin and 90% still showing minimal acne. These findings suggest that the topical plus laser combination provides the fastest and most sustained clinical improvement at week 8.

Statistically, changes in skin condition based on IGA scores from baseline to week 12 were significant across all treatment groups, as confirmed by the Chi-Square test ($p < 0.05$). This showed that while all treatment regimens were effective in the long term, the topical plus laser treatment provided faster and more consistent results, with all participants in this group achieving clear skin as early as week 4 and maintaining it through to week 12.

No	Characteristic	Topical		Systemic + Topical		Laser + Topical	
		n	%	n	%	n	%
1	**IGA at baseline**						
	Clear skin	0	0,0	0	0,0	0	0,0
	The skin is almost unchanged	0	0,0	0	0,0	0	0,0
	Mild severity	22	73,3	3	10,0	0	0,0
	Moderate severity	7	23,3	27	90,0	7	23,3
	Severe severity	1	3,3	0	0,0	23	76,7
	Total	**30**	**100,0**	**30**	**100,0**	**30**	**100,0**
2	**IGA at two –weeks**						
	Clear skin	0	0,0	0	0,0	0	0,0
	The skin is almost unchanged	1	3,3	1	3,3	4	13,3
	Mild severity	28	93,3	29	96,7	20	66,7
	Moderate severity	1	3,3	0	0,0	6	20,0
	Severe severity	0	0,0	0	0,0	0	0,0
	Total	**30**	**100,0**	**30**	**100,0**	**30**	**100,0**
3	**IGA at four – weeks**						
	Clear skin	0	0,0	0	0,0	9	30,0
	The skin is almost unchanged	24	80,0	20	66,7	21	70,0
	Mild severity	6	20,0	10	33,3	0	0,0
	Moderate severity	0	0,0	0	0,0	0	0,0
	Severe severity	0	0,0	0	0,0	0	0,0
	Total	**30**	**100,0**	**30**	**100,0**	**30**	**100,0**
4	**IGA at eight- weeks**						

	Clear skin	3	10,0	10	33,3	30	100,0
	The skin is almost unchanged	27	90,0	19	63,3	0	0,0
	Mild severity	0	0,0	0	0,0	0	0,0
	Moderate severity	0	0,0	0	0,0	0	0,0
	Severe severity	0	0,0	0	0,0	0	0,0
	Total	**30**	**100,0**	**30**	**100,0**	**30**	**100,0**
5	**IGA at twelve – weeks**						
	Clear skin	30	100,0	29	96,7	30	100,0
	The skin is almost unchanged	0	0,0	1	3,3	0	0,0
	Mild severity	0	0,0	0	0,0	0	0,0
	Moderate severity	0	0,0	0	0,0	0	0,0
	Severe severity	0	0,0	0	0,0	0	0,0
	Total	**30**	**100,0**	**30**	**100,0**	**30**	**100,0**

Table 5. Descriptive data for Pre-Post Intervention IGA Score

	Group Treatment	N	Mean Rank	Chi-Square	P-value
Baseline	Topical only	30	23.50	57.974	0.00
	SystemicTopical	30	42.20		
	LaserTopical	30	70.80		
	Total	90			
Week2	Topical only	30	43.98	10.179	0.00
	SystemicTopical	30	41.12		
	LaserTopical	30	51.40		
	Total	90			
Week4	Topical only	30	58.00	71.859	0.00
	SystemicTopical	30	63.00		
	LaserTopical	30	15.50		
	Total	90			
Week8	Topical only	30	50.50	53.990	0.00
	SystemicTopical	30	64.00		
	LaserTopical	30	22.00		
	Total	90			

Table 6 Ranks of IGA score for each treatment group.

The mean change in IGA scores across the three treatment groups was analyzed by using the Kruskal-Wallis test. The results demonstrated a consistent and significant improvement in acne severity for all groups from baseline to week 8, with substantial differences among the treatment groups (Group

Treatment) based on their Mean Ranks. The sample size in each group (N) was analyzed, and varying mean ranks indicated differences in the effectiveness of the treatments. A high Chi-Square value accompanied by a $p < 0.001$ suggests that the differences observed are statistically significant. Therefore, the type of treatment administered has a meaningful impact on the measured outcome.

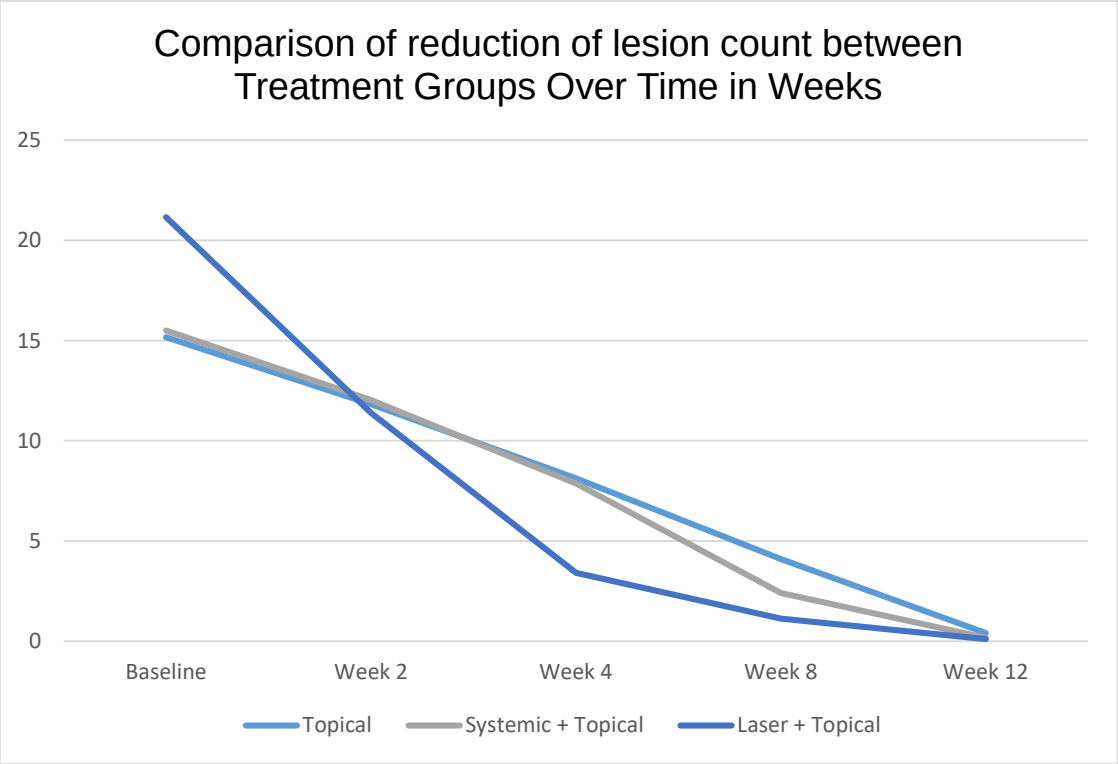

Figure 1. This figure shows the reduction of lesion counts for different treatment groups. It shows that the reduction of lesion count is more rapid in topical plus laser at week 4 compared to topical only and topical plus systemic.

DISCUSSION

This study compared the effectiveness of topical plus laser treatment, against conventional treatment, which were topical alone and topical plus systemic treatment for treating acne vulgaris. Previous research mainly compared only two types of treatments, such as topical vs. topical, topical plus systemic vs. topical plus systemic, or topical plus laser vs. other laser combinations or systemic treatments (Apoorva et al., 2020, 2020; Dhaher & Yosif, 2022; Dogra et al., 2021; Hayashi et al., 2018; Khan et al., 2022; Mohamed et al., 2016; Penna et al., 2014; Sapra et al., 2022; Stein Gold et al., 2022). Besides, this study also used real-world data as we prospectively followed-up the patients who chose their own treatment, providing consistent data collection and reducing risk of recall bias from the patients.

IGA scores and lesion count were measured at the start of treatment and after a specific period to assess changes in the patient's skin condition. Based on IGA, although all treatments significantly improved acne lesions over 12 weeks, the topical plus laser group showed the fastest improvement in more consistent results, where the patients achieved clear skin by week 4 and maintained this state until week 12. The topical plus laser was also the most effective as it reduced the mean lesion count from 21.17 to

0.10, followed by topical plus systemic (0.17) and, lastly, by topical therapy alone (0.40). This indicates that laser therapy is the most effective in accelerating recovery than topical plus systemic therapy and lastly followed by topical treatment alone.

Topical medications are the first-line treatment for mild to moderate acne. These medications include benzoyl peroxide (BPO), salicylic acid, niacinamide, azelaic acid, topical retinoids such as tretinoin, adapalene, tazarotene, and topical antibiotics such as clindamycin, erythromycin, and minocycline. For mild acne, topical monotherapy is used, but combination therapy of two or more different agents is often prescribed especially when topical antibiotics are prescribed to reduce bacterial resistance, or in patients with moderate to severe acne (Malaysian Health Technology Assessment Section (MaHTAS), 2022). Regarding their mechanism of action, BPO has comedolytic and bactericidal properties by killing C. acne, salicylic acid works by exfoliating the skin and keeping the pores clean thereby preventing blockage, niacinamide reduces sebum secretion and protects the skin from acne, and azelaic acid has antibacterial, anti-inflammatory, keratolytic, and antioxidant properties (Vasam et al., 2023). Topical retinoids as a group provide therapeutic effects through several mechanisms such as reducing sebum production, controlling comedone formation, repairing the epithelial layer, and treating hyperpigmentation and scarring (Vasam et al., 2023).

If the patient does not respond well to topical treatments, has moderate to severe acne, or has nodular acne, systemic treatments are the next step in management. These include oral isotretinoin, hormonal medications such as estrogen plus progesterone combinations and spironolactone, and oral antibiotics such as tetracycline, doxycycline, minocycline, erythromycin, and azithromycin (Malaysian Health Technology Assessment Section (MaHTAS), 2022). Of these medications, isotretinoin is the most effective agent because it targets all of the pathophysiology of acne. However, the limitations of isotretinoin are that it can cause some serious side effects that require close monitoring and should not be used in women who are pregnant or planning to become pregnant (Malaysian Health Technology Assessment Section (MaHTAS), 2022; Vasam et al., 2023).

Meanwhile, the Nd: YAG laser treats acne through several mechanisms. First, it penetrates the dermal layer of the skin. It focuses its photothermal effect on the hyperactive sebaceous glands, causing sebaceous gland damage and reducing sebum production, which in turn reduces the Cutibacterium acnes population (Moftah & Moftah, 2022; Xu et al., 2025). Second, it controls the inflammatory process by reducing relevant cytokines through reducing interleukin-8, leading to reduced neutrophil-driven inflammation, reducing Toll-like receptor 2, which triggers microbial immune responses, and also increasing transforming growth factor-b, which promotes resolution of inflammation and inhibits microcomedone formation (Moftah & Moftah, 2022; Xu et al., 2025). Third, it reduces perifollicular hyperkeratinization by thinning the stratum corneum and follicular epithelium, which reduces follicular blockage. This promotes normal follicle turnover and prevents comedone formation (Xu et al., 2025). Fourth, it modifies local lipid metabolism and the microenvironment of the pilosebaceous unit. By reducing sebum production, it suppresses the proliferation of the virulent C. acnes phylotype IA1, which thrives in lipid-accessible anaerobic environments (Xu et al., 2025).

In this study, all patients who received topical treatment were prescribed a fixed-dose combination of topical medications, few of the formulation contained two medications and few contained three medications in a single application. Although this group did not benefit from the additional effects of systemic and laser treatments, and the rate of clinical resolution was the slowest compared to topical plus systemic and topical plus laser treatments, topical treatment was still shown to be very beneficial for patients with mild to moderate acne because it still showed stable and statistically significant

reduction in acne lesions and improvement in IGA scores at 12 weeks of treatment. This highlights the importance of using combined topical treatments, especially fixed-dose combinations, rather than using separate topical applications, let alone topical monotherapy.

Wiraputranto et al., (2024) had retrospectively reviewed 131 patients with mild to severe acne receiving standard acne vulgaris treatment over 12 weeks based on the clinical practice guideline in Indonesia. The patients received treatment based on their acne severity, consisting of topical retinoic acid, BPO, topical antibiotic like clindamycin, oral antibiotic like doxycycline, topical azelaic acid. Majority of them received a combination of retinoic acid plus BPO plus topical or oral antibiotics. The finding showed that there was significant reduction of total lesion count by 77%, non-inflammatory lesion by 71%, and inflammatory lesion by 82%. Mild acne patients also increased from 20.6% from the initial treatment to 93.1% after 12 weeks of treatment. The author attributed the success of the treatment to strict adherence to the clinical guideline, effective combination therapy, good patient education and support, and the use of adjuvant treatment like chemical peels, comedone extraction, light and laser therapy and dermocosmetic (Wiraputranto et al., 2024).

A few other studies also support the finding of the effectiveness of combined topical medication in this study. The higher efficacy of combined medicines is because they target multiple pathways of acne pathogenesis simultaneously, rather than targeting one pathogenesis only. Dogra et al., (2021) had compared a fixed dose combination of tretinoin microspheres 0.04% plus clindamycin 1% versus tretinoin 0.025% alone and clindamycin 1% alone and assessed the clinical efficacy over 12 weeks of treatment. The author showed that combined tretinoin microspheres 0.04% plus clindamycin 1% therapy was significantly more efficacious than monotherapy medication in reducing inflammatory, non-inflammatory, and total lesions and improving IGA score. Besides, this combined medication has the fastest onset, exhibits the earliest reduction of several lesions and has higher tolerability than monotherapy medications (Dogra et al., 2021). The clindamycin reduces the C. acnes proliferation and inflammation in this combination while the tretinoin 0.04% microsphere normalises follicular keratinisation, promotes comedolytic, and enhances skin turnover. Besides, combined medication exert synergistic effects on each other, where tretinoin enhances clindamycin penetration into the pilosebaceous unit, making the antibiotic more effective (Dogra et al., 2021).

Another factor that influences the efficacy of topical medication is whether the medication is a fixed-dose combination or a combination of separate applications of monotherapy medication. Hayashi et al., (2018) had conducted a randomised controlled trial to compare the difference in efficacy and practicality between a fixed-dose combination of clindamycin phosphate/ Benzoyl peroxide (CLNP/BPO) 3% gel vs a combination of separate application of adapalene (ADA) plus CLNP over 12 weeks. They proved that a fixed-dose combination of CLNP/BPO 3% has the greater reduction of inflammatory lesion count compared to the separate application of ADA plus CLNP at week 2 of treatment. Throughout the 12 weeks, although both groups continued to show improvement over time, CLNP/BPO still showed superiority over ADA plus CLNP (Hayashi et al., 2018). Beside synergistic effect of antibacterial properties and anti-inflammatory of BPO and clindamycin and faster effect of BPO than ADA, the adherence rate was higher in the combined medication due to easier application and comfort, making the patient more likely continuing to take the medication throughout the treatment course compared to separate medication. Additionally, adverse reactions occurred less frequently among patients receiving CLNP/BPO 3% than ADA plus CLNP, potentially increasing adherence rate (Hayashi et al., 2018).

Adding more medication in a single fixed-dose combination will increase the efficacy of the treatment as more acne pathogenesis are tackled. Stein Gold et al., (2022) compared the clinical efficacy of triple combination (fixed-dose topical CLNP 1.2%/BPO 3.1%/ADA 0.15% (IDP-126) versus three types of dual combination drugs which were BPO 3.1%/ADA 0.15% gel, CLNP 1.2%/BPO 3.1% gel, CLNP 1.2%/ADA 0.15% gel, as well as the vehicle over 12 weeks. In this study, patients receiving the triple combination had higher clinical improvement as compared with dual combination and vehicle alone. Besides, the IDP-126 also had the highest reduction of inflammatory lesion and non-inflammatory lesions over 12 weeks compared to other treatment, 1.7 to 1.8 times more effective than two drugs combinations, and exhibited the earliest onset of action by week 2 of treatment and consistently showed through week 4, 8, and 12. This is again the synergistic effect in IDP-126 which enhance the efficacy of each treatment, where the ADA halted excess sebum production, comedone formation, follicular hyperkeratinization and inflammation, the CLNP reduced the inflammation and C. acnes bacterial colonisation, and BPO poses antibacterial properties against the C. acnes and comedolytic properties (Stein Gold et al., 2022). The combination treatment also is simpler to use because it only requires a single daily application which minimises treatment complexities and improves treatment adherence. Besides, the technology of IDP-126 also one of the factor of its higher efficacy as polymeric technology provide more uniform distribution of all ingredients, and the BPO and adapalene have been micronised providing smaller particles which enable the the drugs to go deeper and more controlled penetration and reducing surface irritation (Stein Gold et al., 2022).

Our study also discovered that a combination of topical plus systemic therapies effectively reduced acne severity, with significant clinical improvement from baseline to the end of treatment. Although both topical plus systemic and topical plus laser treatment ultimately achieved similar outcomes, which is clear skin by week 12, topical plus systemic therapy showed a slower response than topical plus laser therapy, which showed earlier improvement. Nonetheless, using topical plus systemic remains relevant and practical, especially for patients with moderate acne who may not be suitable for laser therapy due to cost, personal preference, or specific health factors. An important implication of this study is the need for personalised treatment selection, based not only on efficacy but also on accessibility.

A combination of topical plus systemic treatment is also the recommended first-line treatment for severe acne. One study had explored the efficacy of the combination of topical plus systemic treatment vs oral isotretinoin alone in treating severe acne, and found that the combination treatment is preferred than isotretinoin monotherapy. This is because isotretinoin is linked to a few potential adverse effects like depression, risk of teratogenicity, requiring intensive lab monitoring and adherence to iPledge program (Kapała et al., 2022; Vasam et al., 2023). Penna et al., (2014), in particular, had compared A-BPO/Doxycycline combination vs oral isotretinoin, where the evidence showed that the combination of A-BPO/ Doxycycline is as effective as oral isotretinoin, safer, and cheaper thus more cost-effective, and, making it preferred agent over isotretinoin. Nevertheless, none of our respondents were prescribed with oral isotretinoin throughout the treatment course.

Studies comparing different types of oral antibiotics plus topical treatments have also been done before which showed different oral antibiotics could give different results. A study on the comparative efficacy between oral azithromycin 500 mg thrice a week plus topical clindamycin 1% gel twice a day vs oral doxycycline 100 mg daily plus topical clindamycin 1% gel twice a day for eight weeks showed that azithromycin treatment had higher symptom-free days of 85 days while doxycycline treatment had only 31 symptom-free days, so the cost per symptom-free day was higher in the doxycycline group (Rs1400) while azithromycin had a lower cost (Rs499) (Apoorva et al., 2020). Khan et al., (2022) compared the efficacy of topical ADA plus oral Azithromycin vs topical ADA plus oral doxycycline among patients

with mild to moderate acne vulgaris. Group A was treated with topical ADA plus oral azithromycin 250 mg daily, while group B was treated with topical ADA plus oral doxycycline 100 mg twice daily for 12 weeks. Both treatments were very well tolerated, and 90% of patients in group A responded to treatment, while only 73% of group B patients responded to treatment, although the difference was not statistically significant. This could be due to lower frequency of azithromycin dose which improves overall compliance, less pills required, leading to lower overall costs but higher efficacy. This suggests that different types of antibiotics also play a role in treatment efficacy, significantly affecting total treatment costs, and may guide physicians to choose a treatment that offers higher symptom-free days and higher cost-effectiveness.

Pertaining to laser treatment, few authors had conducted a study evaluating the efficacy of laser on acne recovery. In general, the laser is highly effective in treating acne especially for this with mild to moderate acne. However, patients with more severe acne might need more sessions with the laser treatment to achieve more satisfactory recovery. For instance, Dhaher & Yosif, (2022) conducted a prospective study evaluating patients with mild to severe acne undergoing treatment with long-pulsed Nd: YAG laser (1064 nm) alone without any adjunctive treatment. All patients received 3 sessions of laser treatment with 2 week intervals between the sessions, and were followed up and assessed at week 8 after final treatment. After the treatment, 80.3% of them had excellent responses while 13.1% had poor responses, especially those with severe acne and 81% of them fully satisfied with the treatment. There was also a significant reduction of total lesions, with baseline mean lesions of 84.2 ± 39.6 to 16 ± 23.3.

In another study, Mohamed et al., (2016) had compared two types of lasers to determine which one is more efficacious and superior in improving acne lesions. Split-face study design was utilised where intense pulse light (IPL) was used to treat half of the face, and the other half was treated with 1064 nm Long pulsed Nd: YAG laser. All patients received 3 treatment sessions within 4 weeks apart, and final assessment was done 4 weeks after the last treatment. There was no concomitant topical or systemic treatment given. The author reported that both treatments significantly reduced the inflammatory lesion where treatment with IPL resulted in 67.1% reduction of the lesion, while the 1064 nm Long pulsed Nd: YAG laser resulted in 70.2% reduction of the lesion. However, the reduction of non-inflammatory lesions were not significant with both treatments, where IPL and Long pulsed Nd: YAG laser reduced the non-inflammatory lesion by 18.3% and 19.3% respectively. Treatment with IPL also reduced the acne severity score from 3.8 to 1.2, while the 1064 nm Long pulsed Nd: YAG laser reduced the score from 3.7 to 0.9. In conclusion, both treatments were efficacious, however no significant difference between both treatment modalities were found.

The efficacy of laser is also amplified when combined with adjunctive treatment like topical medications or systemic medications as depicted in our study, and most efficacious when combined with oral isotretinoin. Olugbade et al., (2025) conducted a retrospective study among mild to severe acne patients who received 650-ms, 1064 Nd: YAG laser. All patients were treated with the laser, and each of them had a median treatment with laser of 3. The patients were also allowed to use topical and systemic medications, as well as physical treatment. BPO, ADA, Azelaic acid, minocycline, and tretinoin were used 265, 125, 77, 52, and various times respectively. While for oral medications, 56.4% of them received oral antibiotics, 17.3% used hormone-modulating therapy, and 26.2% of them did not receive any oral medication. 87 patients had undergone chemical peels, 14 patients underwent comedone extractions, and few patients received silkpeel or bluelight procedures. The results showed that 48% of patients had achieved full clearance after a median of 3 sessions and the IGA score improved from a median of 3 to 1 at 6 months post-treatment. Treatment with laser also exhibited sustained results,

as many patients remained clear months after their last session. 80% of them also did not use isotretinoin, indicating that laser alone or with topical or oral medication was sufficient to control the acne. In another study, Sapra et al., (2022) had retrospectively examined the safety and effectiveness of using oral isotretinoin plus multiplex pulsed dye laser (PDL) and Nd: YAG laser among those with moderate to severe acne vulgaris. In this study, all patients received oral isotretinoin with varying starting and maintenance doses, and all of them received the laser treatment, whether during isotretinoin treatment, during and after isotretinoin treatment, and only after isotretinoin finished. This study showed that 99.2% of them had clear or almost clear skin at the end of treatment, and concomitant treatments of isotretinoin and lasers were safe with no serious side effects.

Research Limitations and recommendation

Despite the favourable result of this study, it is not without limitation. This study utilised non-randomised study design, where the patients self-selected the treatment regime after thorough assessment by the treating doctor, potentially introducing selection bias. As the patients select different treatments, they might have different levels of motivation, income, and acne severity which could affect the comparison between different treatment groups. Besides, this study also utilised convenience sampling which limits the generalisability of the finding. It did not represent a broader acne vulgaris population across different regions, age groups, or other comorbidities.

Next, neither the patients or doctors were blinded to the treatment regime. This could influence patient reporting outcome and clinical assessment of acne severity as well as lesion count, increasing the risk of detection and performance bias. Plus, other factors that could influence acne like dietary habits, skincare routines, hormonal status and compliances were also not strictly controlled during the study. In addition, this study also observed the treatment outcomes for only 12 weeks. This duration may be adequate to see the short term effect of the treatment for acne, however, it could not capture the long term effect of the treatment like relapse rates, scar prevention, and sustained efficacy.

Different treatment regimens were also performed at different clinics. Variations in physician expertise, patient demographics, and clinic protocols may confound the results and introduce institutional or practitioner variability that may affect treatment outcomes. In addition, sample sizes per treatment group were small, insufficient to detect small but clinically important differences or to generalize findings to the broader population. The small number of patients also affected subgroup analyses across acne severity. Finally, within each treatment group, there were multiple topical and systemic agents grouped as topical alone, topical plus systemic, or topical plus laser, which increases the ability to attribute results to specific combinations.

There are several recommendations for further research, namely using a randomized, controlled and blinded design method. This method will minimize selection, detection, and performance bias, strengthen internal validity, and allow for a more precise comparison of treatment effectiveness.

Besides, the future study should also implement standardised treatment protocols and control confounding variables. Uniform treatment protocols within each group, like similar topical or systemic agents, should be applied to ensure clearer attribution of outcomes and whether the treatment efficacy is due to the specific agent. Additionally, other confounding factors of acne, like patients' diet, skincare routines, hormonal status, and adherence to the treatment, should be recorded and controlled to enhance the reliability of the findings.

Furthermore, future studies should also recruit larger sample sizes and more diverse patient populations across regions, age groups, and comorbidities to increase the generalizability of the findings. Lastly, longer follow-up is also recommended to evaluate the long-term effects of treatments not covered in this study, such as recurrence rates, scarring, and long-term patient satisfaction. This will provide more comprehensive insights into each treatment modality's durability and efficacy.

Conclusion

The study revealed that all treatment modalities effectively treated acne over a 12-week week. However, Laser combined with topical treatment had the most rapid and consistent clinical improvement, while topical and topical plus systemic treatment had slower improvement

The higher improvement rate in topical plus laser treatment suggests that although this treatment has a higher initial cost, it provides better cost-effectiveness through shorter treatment duration, fewer clinic visits, and potentially lower psychosocial stress on acne because improvement is seen earlier. However, this study has several limitations, including the non-randomized design, potential selection bias and demographic imbalances across treatment groups. These limitations may affect the generalizability of the study results.

In summary, although all treatment options showed good results at 12 weeks, laser combined with topical therapy appeared to provide better benefits in treating acne. Future trials using randomized controlled trials with larger sample sizes and diverse demographics will allow us to evaluate laser therapy's long-term effectiveness and cost-efficiency in treating acne vulgaris.

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