

Effectiveness of Topical Microbiome Containing Lactococcus Ferment Lysate 5% in Acne Vulgaris Patients

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Abstract

Background: Acne vulgaris is a type of persistent inflammatory dermatosis and can be manifested on varying levels, ranging from mild to very severe, but even moderate cases can cause psychological and emotional suffering. Several skin microbiomes are involved in the pathophysiology of acne vulgaris, and alterations in the microbiome composition (dysbiosis) will contribute to the breakdown of the skin barrier as well as immunological activation and inflammation. Lactococcus ferment lysate is a probiotic that has been shown to have anti-inflammatory properties. Topical probiotic treatments are considered safe and without adverse effects, when compared to topical and systemic standard therapies.

Objective: The purpose of this study was to investigate the efficacy of treating acne vulgaris with a microbiome comprising 5% Lactococcus ferment lysate.

Methods: The study employed a double-blind randomized controlled trial design. A total of 70 research participants were separated into two groups: placebo (A) and therapy (B). To determine the correlation between the two variables, the Pearson correlation test was used.

Results: The average number of lesions in the intervention group decreased from 48.5 (before intervention) to 24.5 (after intervention). Furthermore, it was discovered that lowering sebum levels on the forehead (week-6) and cheeks (week-8) was more effective in the intervention group than in the control group (placebo). Pro-inflammatory cytokines (IL-12, IL-8, and TNF- α) decreased in both the treatment and placebo groups, but not significantly ($P > 0.05$).

Conclusion: It has been demonstrated that topical microbiomes containing 5% Lactococcus ferment lysate lower the severity of acne vulgaris, sebum levels, pro-inflammatory cytokines, and enhance anti-inflammatory cytokines.

Keywords: Acne vulgaris, Lactococcus ferment lysate, microbiome, topical probiotic.

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Introduction

Acne vulgaris is a chronic inflammatory dermatosis that manifests as both non-inflammatory and inflammatory lesions.¹ Recent research into the pathogenesis of acne vulgaris has focused on the anti-inflammatory activities of the skin microbiota.² Changes in the composition of the microbiota, or dysbiosis, can disrupt the epidermal barrier, causing the immune system to activate and an inflammatory process to begin.²

The use of antibiotics as the main treatment for acne has resulted in increased resistance to Cutibacterium acnes (*C. acnes*).³ Recent findings regarding the pathophysiology of acne involving dysbiosis of the microbiota have shifted the goal of acne treatment to restore the balance of the natural microbiome.²

Lactococcus ferment lysate is a form of probiotic that can affect the skin microbiome and has an anti-inflammatory effect. Anggraeni et al, repor-

ted in her study that administration of probiotic 5% *Lactococcus lactis* in cases of acne vulgaris could reduce *C. acnes* colonization and the degree of lesion severity.⁴ This study aims to determine the effectiveness of using a microbiome containing 5% *Lactococcus ferment lysate* for acne vulgaris patients.

Methods

This study is an experimental research with a double-blind, pre- and post-treatment randomized controlled clinical trial design conducted at the Department of Dermatology & Venereology, Rumah Sakit Universitas Hasanuddin, Makassar, South Sulawesi, Indonesia during Januari 2022 to Januari 2023. This study was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Hasanuddin, Makassar, with number 47/UN4.6.4.5.31/PP36/2022.

The 70 participants in this study were placed into two groups: placebo (Group A) and treatment/intervention (Group B). Research subjects who met the inclusion and exclusion criteria were obtained from the results of history taking and physical examination. At the first visit (week 0), data was collected which included the degree of severity of acne vulgaris and removal of come-

done on the face to measure levels of interleukin-12 (IL-12), interleukin-8 (IL-8), tumor necrosis factor- α (TNF- α), and interleukin-10 (IL-10) cytokines prior to administration of therapy. Subjects were then randomly assigned to the study group. If the patient is in the placebo group, they will be given face wash and placebo gel, whereas if the subject is in the treatment group, they will receive face wash soap and gel containing 5% *Lactococcus ferment lysate*. The gel is used for 8 weeks. At the second, third and fourth visits with a span of two weeks an assessment of clinical improvement was carried out by counting the number of lesions. At the fifth visit (week 8) an assessment was made of clinical improvement and measurement of IL-12, IL-8, TNF- α , and IL-10 levels after administration of therapy.

The data was analyzed using SPSS version 22. A paired T-test was used to compare subject groups' observations from two or more samplings.

Results

The study was conducted on 77 research subjects who met the inclusion and exclusion criteria, however, 7 subjects dropped out, leaving 70 research subjects.

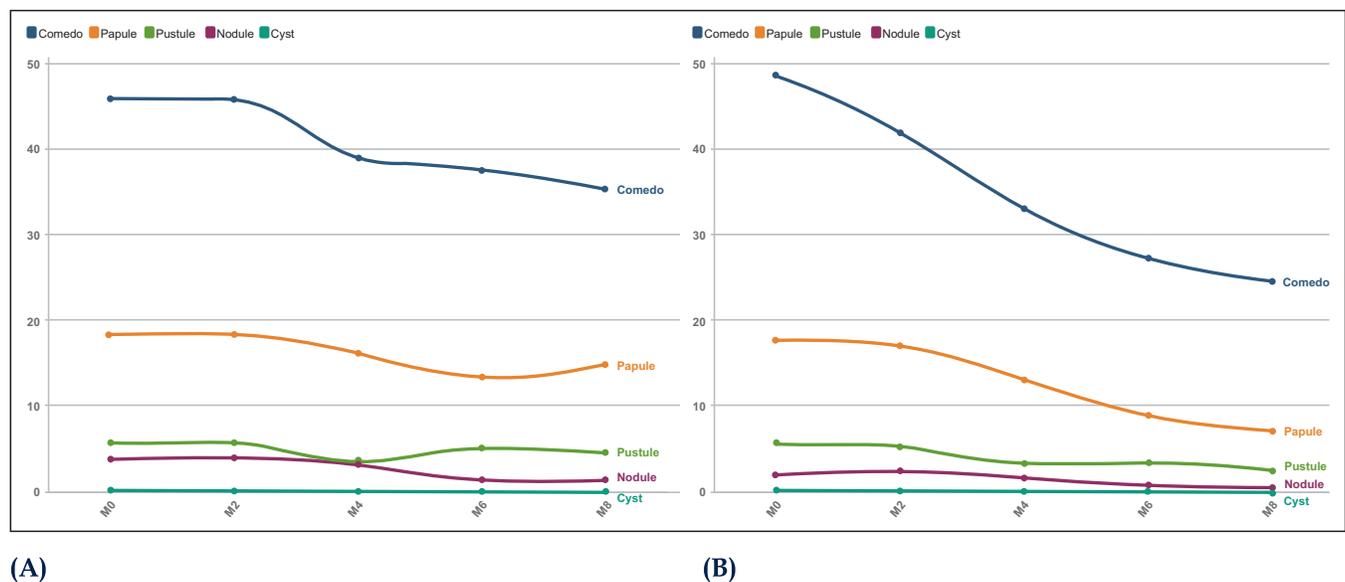


Figure 1: Decrease in the number of each type of lesion in the placebo (A) and treatment (B).

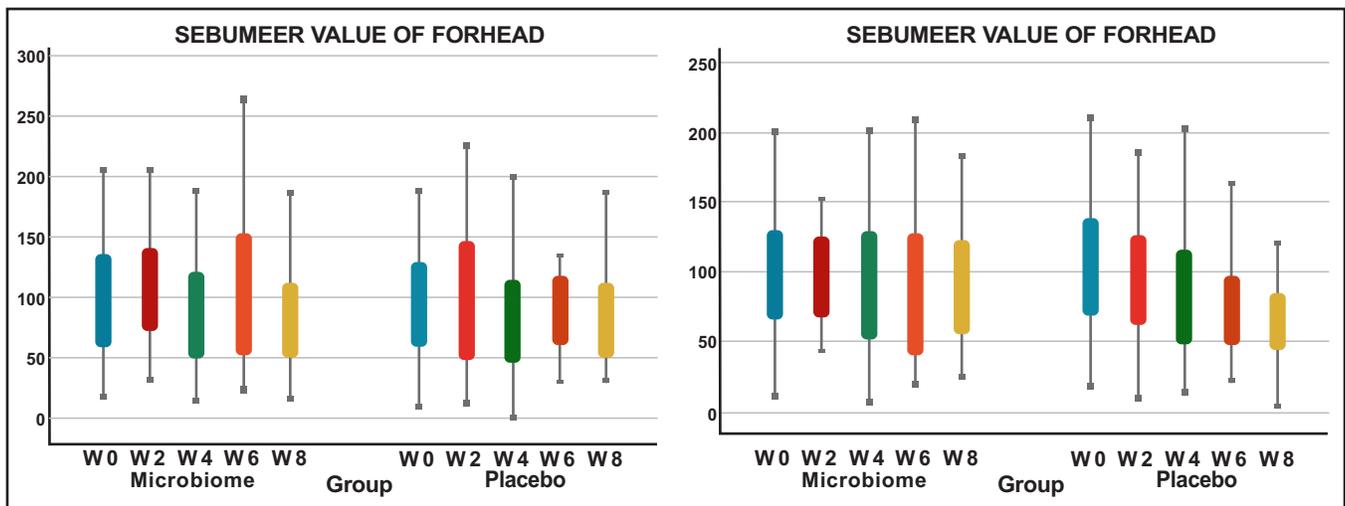


Figure 2: Comparison of sebum levels in the two treatment groups.

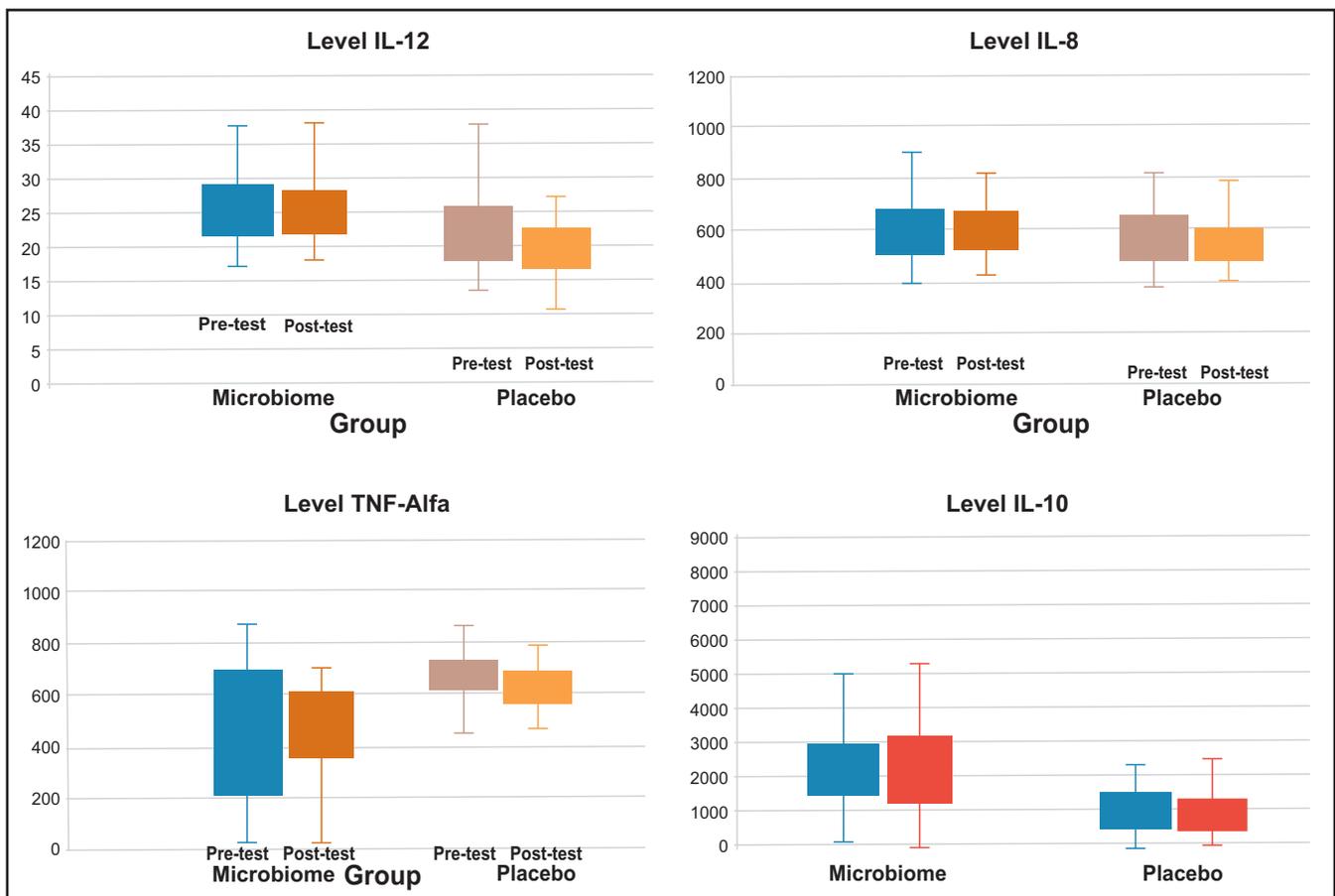


Figure 3: Comparison of cytokine levels before and after giving interventions (boxplot).

The reduction in lesions in the placebo and therapy groups was classified based on the kind of lesion. The greatest decrease in both groups was found in comedo lesions, with the placebo group

having 35.4 lesions at the end of the observation compared to the average number of initial lesions of 45.9 (Figure 1) and the treatment group having 24.5 lesions at the end of the observation compar-

ed to the average number of initial lesions of 48.5 (Figure 2).

The treatment group was more effective in reducing sebum levels in the forehead area based on the results of sebum levels on the right cheek, left cheek, and forehead in both groups. From week 0 to week 6, there was no difference in cheek area sebum levels between the two groups. There was a substantial difference in cheek area sebum levels in the treatment group at week 8.

When comparing observations to baseline levels, there was a decrease in pro-inflammatory cytokines (IL-12, IL-8, and TNF- α) and an increase in anti-inflammatory cytokines (IL-10) in both groups, but these changes in values were not statistically significant ($p > 0.05$) (Figure 3 and Table 1).

Discussion

Acne vulgaris is a chronic pilosebaceous unit inflammation caused by both intrinsic and external causes. The pathogenesis of acne vulgaris involves excess sebum production, abnormal follicular keratinization, proliferation of *C. acnes*, and inflammatory processes.¹ In a balanced microbiome, *Staphylococcus epidermidis* (*S. epidermidis*) can limit the over-colonization and skin inflammatory response elicited by *C. acnes*. The balance of the microbiome in the skin can maintain the skin barrier and reduce inflammatory activity in the skin.⁵

Table 1. Comparison of cytokine levels before and after the intervention.

			N	Mean	SD	p-value*
IL-12	Microbiome	Pre test	35	25.373	57.84	0.801
		Post test		23.37	55.23	
	Placebo	Pre test	35	23.370	62.59	0.300
		Post test		24.94	56.06	

*T test dependent

			N	Mean	SD	p-value*
IL-8	Microbiome	Pre test	35	584.53	132.90	0.55
		Post test		603.44	130.01	
	Placebo	Pre test	35	564.51	129.64	0.984
		Post test		563.87	129.15	

*T test dependent

			N	Median	Max	Min	p-value*
TNF- α	Microbiome	Pre test	35	584	840	0	0.600
		Post test		567.7	681.7	0	
	Placebo	Pre test	35	669.7	857.45	75.85	0.72
		Post test		24.94	995.68	35.05	

*Wilcoxon

			N	Median	Max	Min	p-value*
IL-10	Microbiome	Pre test	35	2245.14	5032.98	250.64	0.608
		Post test		2472.61	5322.97	96.72	
	Placebo	Pre test	35	1317.37	2436.04	96.95	0.610
		Post test		1139.29	7829.61	135.65	

*Wilcoxon

In this study, both the placebo and therapy groups experienced improvements in acne vulgaris lesions. The placebo group experienced a faster reduction in the number of lesions, which occurred in week 2 for both inflammatory and non-inflammatory lesions. In the treated group, non-inflammatory lesions decreased at week 4 and inflammatory lesions decreased at week 6. According to the findings of this study, administering 5% Lactococcus ferment lysate has a better effect on long-term use. The findings of this study are similar to those of Anggraeni et al, who investiga-

ted the use of long-term *Lactococcus lactis* microbiome therapy in acne vulgaris. Acne vulgaris sufferers receive topical sunscreen and probiotic treatment for 8 weeks and there is an improvement in the condition of the facial skin to become smoother and more hydrated.⁴

Sebum reduction was more effective in the forehead and cheek areas in the treatment group in this study. Acne sufferers tend to secrete more sebum than people without acne and the level of secretion has been shown to correlate with the severity of the lesion.⁶ Topical microbiome administration has a higher concentration in target organs than oral administration. A study showed an increase in skin barrier function after topical administration of *Lactococcus ferment lysate*.⁷ *Lactococcus ferment lysate* can stimulate the expression of antimicrobial protein β -defensin-2 in the skin which is important for defense against skin pathogens such as *Staphylococcus aureus* (*S. aureus*), *Streptococcus pyogenes* (*S. pyogenes*) and *Candida albicans* (*C. albicans*).^{4,8,9,13}

Interleukin-10 (IL-10) reduces the expression of MHC class II and the costimulatory protein B7-1/B7-2 in monocytes and macrophages, as well as the production of proinflammatory cytokines.^{9,10} Interleukin-10 levels in the treatment group increased due to the basic function of IL-10 as an immunoregulator in inflammatory conditions.¹⁴⁻¹⁸ Increasing IL-10 levels in the treatment group can be optimized by adjusting the levels of *Lactococcus ferment lysate* contained in it or adding other active ingredients to the topical therapy design. This can be a consideration for further research on alternative therapies for acne vulgaris.

Conclusion

Topical microbiomes containing 5% *Lactococcus ferment lysate* have been proven to lower the severity of acne vulgaris, sebum levels, pro-inflammatory cytokines, and enhance anti-inflammatory cytokines.

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Author's Contribution

AIA: Conception & design, acquisition of data, critical revision of the article, drafting of article.

AAZ: Conception & design, analysis & interpretation, final approval of the version to be published

ENH: Acquisition of data, drafting of article, analysis & interpretation of data, drafting of article

KAPS: Drafting of article, final approval of the version to be published.

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