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The effects of cetylpyridinium chloride mouthwash combined with triamcinolone acetonide on oral microbiota and the Th17/Treg balance in patients with oral lichen planus

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Abstract: **Background**: Oral lichen planus (OLP) is a chronic inflammatory disease associated with oral microbiome imbalance and immune dysregulation. **Objectives**: To evaluate the effects of CPC mouthwash combined with triamcinolone acetonide on oral microbiota and Th17/Treg balance in erosive OLP patients. **Methods**: This study involved 80 patients with erosive OLP from January 2023 to January 2025. They were divided into: A control group treated with triamcinolone acetonide and a combination group treated with triamcinolone acetonide plus cetylpyridinium chloride mouthwash. After 4 weeks, primary outcomes included clinical efficacy, visual analog scale (VAS) pain scores, changes in signs and erosive area, oral salivary bacteria detection rate, Th17/Treg ratio, serum adipokine chemerin and cytokine levels (IL-17, TNF-α, IL-10) and OHIP-14 scores. Secondary outcomes were adverse reaction incidence and recurrence rates during follow-up. **Results**: The combination group showed better outcomes after 4 weeks of treatment. The total effective rate was 95%, higher than the control group's 80% (P=0.022). The combination group had superior pain relief (P=0.024), better mucosal repair (P=0.002) and a significant decrease in erosive area (P=0.021). It also had lower oral detection rates of *Staphylococcus* and *Candida albicans* (P<0.05). Immunologically, the combination therapy significantly reduced serum levels of chemerin, Th17 cells, Th17/Treg ratio, IL-17 and TNF-α (P<0.001), while increasing Treg cells and IL-10 levels (P=0.003), indicating stronger anti-inflammatory and immune-balancing effects. The combination group showed a greater reduction in the OHIP-14 score ($P < 0.001$), indicating improved oral health-related quality of life. No significant difference in adverse reactions was observed (P>0.05) and all were mild. The combination group had a lower recurrence rate within 3 months post-treatment, although the difference was not statistically significant (P=0.521). **Conclusion**: The combination of cetylpyridinium chloride mouthwash with triamcinolone acetonide effectively regulates the oral microbiota structure and restores the Th17/Treg immune balance in OLP patients.

Keywords: Cetylpyridinium chloride; Immune regulation; Oral lichen planus; Oral microbiota; Triamcinolone acetonide; Th17/Treg balance

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INTRODUCTION

In 1869, British dermatologist Erasmus Wilson first reported the disease lichen planus (LP) (Tekin *et al.*, 2024). As an immune-mediated chronic inflammatory disease, LP primarily affects ectodermal tissues like skin, mucosa, nails and hair, with a rare risk of malignancy (Vicic *et al.*, 2023). As a chronic immune-mediated condition, oral lichen planus (OLP) specifically targets the oral mucosa and is classified as the mucosal variant of lichen planus. It is characterized by typical chronic and relapsing features, with clinical manifestations alternating between recurrent lesions and periods of remission (El-Howati *et al.*, 2023; Louisy *et al.*, 2024). OLP lesions most often affect the bilateral buccal mucosae, followed by the dorsal tongue, gingivae, and labial mucosae, whereas the hard palate, floor of the mouth and upper lip are less commonly involved (Manchanda *et al.*, 2024). Epidemiological investigations have indicated that OLP affects approximately 1.01% of the global population, with Europe showing the highest incidence rates and India the lowest and the prevalence increases significantly and continuously with age starting from 40 years old (Gonzalez-Moles *et al.*, 2021). In clinical settings, OLP presents with six distinct morphological variants: reticular, plaque-like, atrophic, erosive/ulcerative, papular and vesicular forms (Petruzzi *et al.*, 2023). The subtypes can appear individually or together, with reticular, erosive/ulcerative and plaque-like forms being most frequent (Gonzalez-Moles and Ramos-Garcia, 2023). Currently, scholars both domestically and internationally primarily classify OLP into erosive and non-erosive types based on clinical manifestations. Non-erosive lesions are predominantly characterized by white or grayish-white striations, whereas erosive lesions, in addition to the classic white lesions, also present with manifestations such as

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congestion, erosion and atrophy (Nukaly *et al.*, 2024). More alarmingly, long-standing erosive lesions have the potential for malignant transformation, with approximately 1.37% of patients developing oral squamous cell carcinoma (Wang *et al.*, 2022). This not only severely affects patients' quality of life but also further exacerbates their psychological burden. To date, the pathogenesis of OLP remains unclear. Factors such as immunity, infection, stress and endocrine factors are all considered potential etiologies, with T-lymphocyte-mediated immune tolerance imbalance believed to play a key role (Yim *et al.*, 2024). In a normal organism, immune tolerance to self-antigens is maintained and immune responses are only elicited against non-self-antigens. However, under internal or external stimuli, the loss of self-immune tolerance leads to inflammatory damage, potentially progressing to the development of autoimmune disease (Reeve *et al.*, 2024).

Recent studies have highlighted the growing significance of oral microecology in autoimmune disorders. For systemic conditions like Sjogren's syndrome, microbial imbalance has been observed, where shifts in microbiota composition correlate with clinical severity, suggesting potential diagnostic utility through oral microbiome analysis (Alam *et al.*, 2020; Li *et al.*, 2020). Similarly, investigations into OLP reveal distinct alterations in microbial diversity compared to healthy controls, underscoring the role of oral flora in its pathogenesis (Deng *et al.*, 2020; Zhong *et al.*, 2020). Baek *et al*. (2020) observed an enrichment of *Escherichia coli* in tissue samples from OLP patients and isolated the E. coli K12 strain from the tissue surface.

Currently, there is no definitive cure for OLP, but its symptoms can be managed, recurrences reduced and malignant transformation prevented through comprehensive treatment strategies (Le Gatt *et al.*, 2023). For asymptomatic patients with non-erosive OLP, active treatment is usually not required; however, regular clinical follow-ups are necessary to monitor disease progression (De Porras-Carrique *et al.*, 2023). Erosive OLP is characterized by recurrent episodes and a prolonged disease course, often lasting several years. Currently, the primary treatment approach for this condition still relies on pharmacological interventions (Lodolo *et al.*, 2023). Triamcinolone acetonide, a medium-potency glucocorticoid, exhibits potent anti-inflammatory, anti-allergic and immunosuppressive effects. By inhibiting the infiltration of inflammatory cells and reducing cytokine production, it effectively alleviates inflammatory responses in the oral mucosa and relieves symptoms such as pain (Alhallak *et al.*, 2024). Despite its favorable anti-inflammatory effects in treating OLP, long-term use of triamcinolone acetonide may lead to adverse reactions, including oral mucosal atrophy and secondary infections (Chaitanya *et al.*, 2022). Moreover, some patients may not respond well to triamcinolone acetonide monotherapy for OLP and the disease tends to relapse after discontinuation of treatment (Salinas-Gilabert *et al.*, 2022). With the deepening of research on the relationship between oral microecology and oral diseases, regulating the oral microbiota to treat oral diseases has gradually emerged as a new research direction. Cetylpyridinium chloride, a cationic surfactant, possesses broad-spectrum antibacterial properties. It can adsorb onto the surface of bacteria, alter the permeability of bacterial cell membranes and cause the leakage of bacterial cytoplasmic contents, thereby achieving bactericidal and bacteriostatic effects (Mao *et al.*, 2020). The antimicrobial mouthwash formulation with cetylpyridinium chloride serves as an effective therapeutic option for various dental conditions, capable of restraining the proliferation of numerous oral pathogenic microorganisms while supporting microbial homeostasis (Riveira-Munoz *et al.*, 2023). Previous studies have demonstrated that cetylpyridinium chloride mouthwash exhibits certain therapeutic efficacy in treating oral inflammatory diseases; however, research on its combined application with triamcinolone acetonide and its impact on the oral microbiota and immune function of OLP patients is relatively scarce (Rajendiran *et al.*, 2021).

Given that the pathogenesis of OLP is closely associated with oral microbiota dysbiosis and immune dysfunction, where microbial shifts may directly or indirectly influence the Th17/Treg equilibrium, as well as the limitations of existing treatment modalities, this study aims to investigate the impact of cetylpyridinium chloride mouthwash combined with triamcinolone acetonide on the oral microbiota and the Th17/Treg balance in OLP patients. Through comparative analysis of pretreatment and posttreatment data, including oral microbiome restructuring, Th17-Treg cell proportion adjustments and peripheral blood cytokine fluctuations, this study evaluates the dual regulatory impact of combination therapy on both microbial balance and immune response. The results are expected to contribute fresh perspectives and clinical solutions for OLP treatment, leading to better patient outcomes and quality of life.

MATERIALS AND METHODS

Research subjects

This was a retrospective observational study analyzing 80 patients with erosive OLP treated between January 2023 and January 2025. Patients were divided into two groups based on the treatment they received: a control group treated with triamcinolone acetonide alone and a combination group treated with triamcinolone acetonide plus cetylpyridinium chloride mouthwash. The assignment to treatment groups was based on clinical decision-making and patient adherence. No randomization, allocation concealment, or blinding was applied, consistent with the observational nature of this study. To control for selection bias and confounders, baseline characteristics including

age, gender, BMI, disease duration, debris index and calculus index were matched between the two groups, as shown in table 1. Additionally, strict inclusion and exclusion criteria were applied to minimize heterogeneity. However, given the non-randomized design, residual confounding cannot be entirely ruled out.

Inclusion criteria: (1) Meeting the diagnostic criteria for OLP set by the World Health Organization (WHO) (Jolehar *et al.*, 2021) and being clinically diagnosed as erosive OLP by dermatology and stomatology experts, with histopathological confirmation; (2) Absence of any systemic diseases, as assessed through a detailed questionnaire based on the revised Cornell Medical Index (CMI) (Pendleton *et al.*, 2004); (3) Aged between 40 and 70 years; (4) A disease course of ≥3 months; (5) Good compliance, being capable of using medications as instructed and completing follow-ups.

Exclusion criteria: (1) Presence of periodontitis or other oral mucosal diseases and tumors; (2) Use of medications affecting the oral microbiota and immune responses, such as antibiotics, steroids and immunosuppressants, within at least 8 weeks prior to the study's initiation; (3) Receipt of any local oral medication within at least 4 weeks prior to the study's start; (4) Suspected lichenoid lesions related to dental prostheses or medications; (5) History of allergy to cetylpyridinium chloride or triamcinolone acetonide; (6) Presence of systemic diseases, such as hypertension and diabetes; (7) Presence of other immune system diseases, such as discoid lupus erythematosus and rheumatoid arthritis; (8) Presence of infectious diseases, such as tuberculosis, hepatitis B and AIDS; (9) Being pregnant or lactating.

Sample size calculation

In this study, the sample size was estimated using the Rosner method (Kim *et al.*, 2017), with calculations performed in G*Power software. The estimation was based on parameters from the research by (Mehdipour *et al.*, 2010). A t-test was planned to compare the differences in erosion area between the two independent groups at the fourth week of treatment. The type I error probability (α) was set at 0.05, and the power (1-β) was set at 0.9. Based on this estimation, a minimum sample size of 68 participants (34 per group) was required. For this experimental study, 80 participants were recruited, which met and exceeded the statistical requirements of the design.

Treatment methods

Among the 80 erosive OLP cases enrolled, half were assigned to receive monotherapy with triamcinolone acetonide (control group), while the other half underwent combination treatment incorporating both triamcinolone acetonide and cetylpyridinium chloride mouthwash (combination group). Patients in the control group applied triamcinolone acetonide oral ointment (produced by Aomei Pharmaceutical Co., Ltd., Hong Kong) three times daily, squeezing an appropriate amount of ointment (approximately 1 cm) onto the erosive or lesional sites. During application, it was essential to ensure that the medication evenly covered the lesional area and to avoid vigorous rubbing, which could exacerbate mucosal damage. Patients in the combination group received the same triamcinolone acetonide treatment as the control group and, in addition, were prescribed cetylpyridinium chloride mouthwash (produced by Sichuan Jianeng Pharmaceutical Co., Ltd.). Each use involved gargling 15 ml of mouthwash for 60 seconds, then spitting it out, three times daily. During gargling, it was crucial to ensure that the mouthwash fully contacted the oral mucosa, particularly the lesional areas. The treatment duration was 4 weeks and patients were required to strictly adhere to the prescribed regimen for both medications, without altering the dosage or discontinuing treatment on their own.

Observation indicators

Primary outcome measures

(1) *Clinical efficacy was evaluated at the end of the 4-week treatment period based on the following criteria (Hwang et al., 2024)*: Complete Response (CR): Complete healing of erosions/ulcerations. The oral mucosa returned to normal or exhibited only slight white striae. Partial Response (PR): Partial healing of erosions/ulcerations. Both symptoms (e.g., pain) and clinical signs showed observable improvement compared to baseline. No response (NR): No significant improvement or worsening of symptoms and clinical signs compared to baseline. The Overall Response Rate was calculated as: (Number of patients with CR + Number of patients with PR) / Total number of patients in the group × 100%.

(2) *Pain severity (Shalaby et al., 2024)*: Assessed using the visual analog scale (VAS). Grade 0 (Painless): VAS score of 0, no pain sensation. Grade 1 (Mild Pain): VAS score of 1-4, slight pain, tolerable, does not affect sleep. Grade 2 (Moderate Pain): VAS score of 5-7, obvious pain but tolerable, partially affects sleep. Grade 3 (Severe Pain): VAS score of 8-10, intense pain, difficult to tolerate, severely affects sleep.

(3) *Grading criteria for symptoms and signs (Abdelsamie et al., 2023)*: Grade 0: No lesions, normal mucosa. Grade 1: Slight white striae, no congestion, atrophy, or erosion. Grade 2: White striae with congestion or atrophy area less than 1 cm^2. Grade 3: White striae with congestion or atrophy area greater than 1 cm^2. Grade 4: White striae with erosion area less than 1 cm^2. Grade 5: White striae with erosion area greater than 1 cm^2.

(4) *Erosion area (Liu et al., 2025)*: Observation of changes in erosion area in OLP patients before and after treatment. The size of the erosion area is measured using a calibrated

periodontal probe and the area is calculated and recorded. Method for calculating erosion area: For irregular shapes, multiply the maximum horizontal diameter by the maximum vertical diameter. For multiple erosive lesions, sum the areas of each lesion.

(5) *Isolation, culture and bacterial identification of oral microorganisms*: Oral saliva samples are collected between meals to avoid interference from food residues. Before collection, subjects are instructed to rinse their mouths thoroughly three times with warm water. Non-stimulated saliva (0.5-1.0 ml) is collected naturally into sterile EP tubes. Oral streptococci and staphylococci are cultured statically in BHI medium at 37°C under 5% CO_2 or anaerobic conditions. *Lactobacilli* are cultured statically in MRS medium at 37°C under 5% CO_2 or anaerobic conditions. Oral *Candida albicans* is cultured in Sabouraud's medium by shaking at 150 r/min or statically on Sabouraud's dextrose agar plates at 37°C. Suspected pathogens such as *Porphyromonas gingivalis*, *Fusobacterium nucleatum* and *Prevotella intermedia* are cultured anaerobically in BHI blood broth medium at 37°C under a mixed gas atmosphere of 80% N_2, 10% H_2 and 10% CO_2. *Aggregatibacter actinomycetemcomitans* is cultured in BHI blood broth medium at 37°C under 5-10% CO_2. Microbiological assessment was based on routine clinical culture methods targeting specific pathogens (*Staphylococcus, Streptococcus, Candida albicans, Lactobacillus, Prevotella intermedia*) and does not represent a full characterization of the oral microbial community. Detection rates (presence/absence) were recorded. This approach does not assess microbial diversity, abundance, or community structure and results should be interpreted as semi-quantitative indicators of specific pathogens rather than as a comprehensive microbiome analysis.

(6) *Laboratory indicators*: The serum samples for serum factor data were derived from surplus serum obtained during routine venipuncture in clinical practice and stored at -80°C. The proportions of immune cell subsets were based on previously performed flow cytometry analyses. The assay workflow is described below: Enzyme-linked immunosorbent assay (ELISA) was used to detect serum levels of the adipokine chemerin and inflammatory cytokines IL-17, TNF-α and IL-10 in both groups before and after treatment. Peripheral blood mononuclear cells (PBMCs) were isolated using density gradient centrifugation (Ficoll-Paque). For flow cytometry analysis, cells were stained with fluorescently labeled antibodies against CD4, CD25, FoxP3 (for Treg identification) and CD4, IL-17 (for Th17 identification) following standard intracellular staining protocols after stimulation with PMA/ionomycin in the presence of brefeldin A. Flow cytometry was performed using a BD FACSCalibur instrument and data were analyzed with FlowJo software (version 10.8.1). Gating strategies were established using fluorescence-minus-one (FMO) controls and results are expressed as percentages of CD4+ T cells. All assays were performed in duplicate and the mean values were used for statistical analysis.

(7) *Quality of life*: Assessed using the Oral Health Impact Profile-14 (OHIP-14) scale (Daume *et al.*, 2020). This tool includes 14 questions assessing four key domains: functional limitations, pain/discomfort, psychological distress and physical impairment.

Secondary outcome measures

(1) *Drug adverse reaction assessment criteria (Zhao et al., 2022)*: During the observation period, which spanned from before the initiation of treatment to 1 month after the completion of the treatment course, adverse reactions that occurred in both groups of subjects were recorded in detail. Adverse reactions were assessed using patient-reported symptoms and clinical examination at follow-up visits. In case of any adverse events, patients were advised to contact the clinic immediately for evaluation. If severe adverse events occurred, the treatment was discontinued and the patient was referred for appropriate medical care. All adverse reactions were documented and analyzed retrospectively.

(2) *Recurrence assessment criteria*: Recurrence is defined as the reappearance of the original subjective symptoms and oral lesion signs in patients who showed a significant therapeutic response during the 3-month follow-up period after drug discontinuation. Non-recurrence is defined as the absence of any original subjective symptoms and oral lesion signs in patients who showed a significant therapeutic response during the 3-month follow-up period after drug discontinuation.

Statistical analysis

In this retrospective study, data completeness was ensured by reviewing all available medical records. Cases with missing primary outcome data were excluded from the respective analyses. No imputation methods were applied, given the observational nature of the study. Statistical processing utilized SPSS 26.0 software. The normality of continuous variables (e.g., erosion area, cytokine values, OHIP-14 scores) was assessed using the Shapiro-Wilk test. Metric variables that followed a normal distribution were compared between groups using the independent samples t-test and reported as mean ± SD. Non-normally distributed metric variables were compared using the Mann-Whitney U test and reported as median (interquartile range). Nominal data (microbial counts, adverse reactions) were presented as n (%) and compared using the χ^2 test or Fisher's exact test as appropriate. Nonparametric analysis (Mann-Whitney U) was used for ranked parameters (therapeutic outcomes, pain severity). Significance thresholds were maintained at $\alpha = 0.05$ for two-tailed tests.

RESULTS

Comparison of general data

Statistical tests on the baseline data of gender, age, body mass index (BMI), disease duration, debris index and calculus index between the two groups revealed no statistically significant differences (P>0.05), indicating that the general demographic characteristics were well-balanced and comparable. See Table 1.

Comparison of the clinical efficacy

After four weeks of treatment, among the 40 patients in the control group, 17 achieved CR, 15 achieved PR and 8 showed NR, resulting in an overall response rate of 80.00%. In contrast, among the 40 patients in the combination therapy group, 26 achieved CR, 12 achieved PR and only 2 showed NR, leading to an overall response rate of 95.00%. When comparing the clinical efficacy between the two groups, a statistically significant difference was observed (Z=2.285, P=0.022). See Table 2.

Comparison of pain degrees

Before treatment, there was no significant difference in the pain severity distribution between the two groups (Z=0.742, P=0.458). After treatment, the combination group demonstrated significantly greater pain relief than the control group (Z=2.253, P=0.024). This indicates that the combination treatment regimen offers greater advantages in alleviating patients' pain, as evidenced by a higher proportion of pain-free patients and lower proportions of patients with mild, moderate and severe pain. See Table 3.

Comparison of changes in clinical signs

Before treatment, both groups predominantly presented with Grade 4 and Grade 5 lesions, with no significant difference observed between the groups (Z=0.154, P=0.650). After treatment, the combination group exhibited more significant improvement, characterized by a higher proportion of patients with Grade 0, Grade 1 and Grade 2 lesions and a lower proportion with Grade 3, Grade 4 and Grade 5 lesions (Z=-3.169, P=0.002). This indicates that the combination therapy is superior to the control treatment in promoting the repair of mucosal lesions, particularly in alleviating moderate to severe erosions. See Table 4.

Comparison of changes in erosion area

Before treatment, the erosion area in the control group was 0.93±0.31 cm², while in the combination group it was 1.04±0.30 cm², with no statistically significant difference observed between the two groups (t=1.618, P=0.110). After treatment, the erosion area in the control group decreased to 0.21±0.43 cm², whereas in the combination group it significantly reduced to 0.04±0.16 cm² (t=2.364, P=0.021). Further analysis of the mean differences revealed that the mean difference in the combination group was 1.00±0.35 cm², significantly higher than the 0.72±0.29 cm² observed in the control group (t=3.888, P<0.001). See Table 5.

Comparison of detection rates for selected oral microorganisms

The detection rates of *Staphylococcus* and *Candida albicans* in the oral cavities of both the control group and the combination group significantly decreased after treatment, with statistical significance (P<0.05). Furthermore, compared to the control group, the combination group exhibited lower detection rates of *Staphylococcus* (χ^2=4.073, P=0.044) and *Candida albicans* (χ^2=4.242, P=0.039) in the oral cavity. Although the detection rates of other salivary bacteria decreased, the differences were not statistically significant (P>0.05). See Table 6 for details.

Comparison of various laboratory indicators

Table 7 compares the levels of inflammatory factors and immune indicators in patients with erosive OLP from both groups before and after treatment. After treatment, the levels of IL-17 and TNF-α in the combination group were significantly lower than those in the control group (P<0.001), while the level of IL-10 was significantly higher (P=0.007). Meanwhile, the chemerin level, the percentage of Th17 cells and the Th17/Treg ratio in the combination group were all significantly lower than those in the control group (P<0.001), whereas the percentage of Treg cells was significantly higher (P=0.003). This indicates that the combination therapy is superior to monotherapy with triamcinolone acetonide in reducing pro-inflammatory factor levels, elevating anti-inflammatory factor levels and regulating the Th17/Treg balance, demonstrating more significant anti-inflammatory and immunomodulatory effects.

Comparison of oral health-related quality of life

Before treatment, the OHIP-14 scores of the control group and the combination group were 16.35±3.19 and 15.88±3.66, respectively, with no statistically significant difference observed between the two groups (t=0.619, P=0.538). After treatment, the OHIP-14 score of the control group decreased to 10.35±2.42, while that of the combination group significantly reduced to 7.25±2.11 (t=6.102, P<0.001). This indicates that the combination therapy is superior to monotherapy with triamcinolone acetonide in improving patients' oral health-related quality of life. See Table 8.

Comparison of adverse drug reaction rates

During the treatment process, one patient in the control group experienced adverse reactions, with an adverse reaction rate of 2.50%, characterized by transient stinging in the local mucosa. In the combination therapy group, two patients experienced adverse reactions, with an adverse reaction rate of 5.00%. One patient presented with mild irritation in the oral pharynx, while the other experienced mild nausea. See Table 9.

Table 1: Comparison of general data ($\bar{x}$±s)

Group	*n*	Gender (male/female)	Age (years)	BMI (kg/m²)	Disease duration (months)	Debris index	Calculus index
Control group	40	15/25	52.65±7.24	23.22±1.52	5.65±1.00	2.30±0.52	2.13±0.41
Combination group	40	17/23	51.85±8.23	23.01±1.44	5.88±1.18	2.23±0.48	2.21±0.41
t/χ^2-value (Independent t-test/χ^2 test)		0.208	0.462	0.658	0.919	0.675	0.803
P-value		0.648	0.646	0.512	0.361	0.502	0.409

Table 2: Comparison of the clinical efficacy [n(%)]

Group	*n*	CR	PR	NR
Control group	40	17 (42.50)	15 (37.50)	8 (20.00)
Combination group	40	26 (65.00)	12 (30.00)	2 (5.00)
Z-value (Mann-Whitney U test)		2.285		
P-value		0.022		
Effect size		0.255		

Table 3: Comparison of pain degrees [n(%)]

Time	Group	*n*	Painless	Mild pain	Moderate pain	Severe pain
Before treatment	Control group	40	0 (0.00)	1 (2.50)	18 (45.00)	21 (52.50)
	Combination group	40	0 (0.00)	2 (5.00)	20 (50.00)	18 (45.00)
	Z-value (Mann-Whitney U test)		0.742			
	P-value		0.458			
	Effect size		0.083			
After treatment	Control group	40	22 (55.00)	11 (27.50)	5 (12.50)	2 (5.00)
	Combination group	40	31 (77.50)	7 (17.50)	2 (5.00)	0 (0.00)
	Z-value (Mann-Whitney U test)		2.253			
	P-value		0.024			
	Effect size		0.252			

Table 4: Comparison of changes in clinical signs [n(%)]

Time	Group	*n*	0	1	2	3	4	5
Before treatment	Control group	40	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	25 (62.50)	15 (37.50)
	Combination group	40	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	23 (57.50)	17 (42.50)
	Z-value (Mann-Whitney U test)		0.154					
	P-value		0.650					
	Effect size		0.017					
After treatment	Control group	40	10 (25.00)	7 (17.50)	8 (20.00)	7 (17.50)	4 (10.00)	4 (10.00)
	Combination group	40	15 (37.50)	11 (27.50)	10 (25.00)	2 (5.00)	2 (5.00)	0 (0.00)
	Z-value (Mann-Whitney U test)		-3.169					
	P-value		0.002					
	Effect size		0.354					

Table 5: Comparison of changes in erosion area ($\bar{x}$±s, cm^2)

Group	*n*	Before treatment	After treatment	Mean difference
Control group	40	0.93±0.31	0.21±0.43	0.72±0.29
Combination group	40	1.04±0.30	0.04±0.16	1.00±0.35
t-value (Independent t-test)		1.618	2.364	3.888
P-value		0.110	0.021	<0.001
Effect size		0.361	0.524	0.871

Table 6: Changes of salivary microbiota [n(%)]

Bacterial species	Before treatment		After treatment	
	Control group (*n*=40)	Combination group (*n*=40)	Control group (*n*=40)	Combination group (*n*=40)
Staphylococcus	35 (87.50)	36 (90.00)	26 (65.00)	17 (42.50)
Streptococcus	32 (80.00)	30 (75.00)	28 (70.00)	26 (65.00)
Candida albicans	32 (80.00)	31 (77.50)	11 (27.50)	3 (7.50)
Lactobacillus	3 (7.50)	2 (5.00)	2 (5.00)	2 (5.00)
Prevotella intermedia	2 (5.00)	3 (7.50)	0 (0.00)	0 (0.00)

Table 7: Comparison of inflammatory factor levels ($\bar{x}$±s, ng/L)

Time	Group	*n*	IL-17	TNF-α	IL-10
Before treatment	Control group	40	0.43±0.10	32.39±5.11	9.34±2.16
	Combination group	40	0.45±0.09	33.41±6.50	9.15±2.51
	t-value (Independent t-test)		1.010	0.780	0.363
	P-value		0.316	0.438	0.718
	Effect size		0.210	0.174	0.081
After treatment	Control group	40	0.26±0.06*	24.21±3.06*	10.89±2.28*
	Combination group	40	0.14±0.05*	18.13±3.25*	12.23±2.05*
	t-value (Independent t-test)		10.361	8.628	2.758
	P-value		<0.001	<0.001	0.007
	Effect size		2.173	1.926	0.618

Note: Compared with before treatment, *P<0.05.

Table 8: Comparison of chemerin and Th17/Treg ratios ($\bar{x}$±s)

Time	Group	*n*	Chemerin (mg/L)	Th17 (%)	Treg (%)	Th17/Treg
Before treatment	Control group	40	0.43±0.10	2.43±0.52	1.85±0.35	1.39±0.51
	Combination group	40	0.45±0.09	2.41±0.41	1.88±0.48	1.40±0.51
	t-value (Independent t-test)		0.885	0.100	0.363	0.072
	P-value		0.379	0.921	0.717	0.943
	Effect size		0.210	0.043	0.071	0.020
After treatment	Control group	40	0.25±0.06*	1.65±0.25*	2.03±0.29*	0.83±0.16*
	Combination group	40	0.14±0.05*	1.16±0.28*	2.23±0.31*	0.53±0.14*
	t-value (Independent t-test)		7.995	8.360	3.073	8.768
	P-value		<0.001	<0.001	0.003	<0.001
	Effect size		1.992	1.846	0.666	1.966

Note: Compared with before treatment, *P<0.05.

Table 9: Comparison of OHIP-14 scores ($\bar{x}$±s, score)

Group	*n*	Before treatment	After treatment
Control group	40	16.35±3.19	10.35±2.42*
Combination group	40	15.88±3.66	7.25±2.11*
t-value (Independent t-test)		0.619	6.102
P-value		0.538	<0.001
Effect size		0.137	1.365

Note: Compared with before treatment, *P<0.05.

Table 10: Comparison of adverse drug reaction rates

Group	n	The number of adverse reactions	Incidence of adverse reactions (%)
Control group	40	1	2.50
Combination group	40	2	5.00
χ^2-value (χ^2 test)			0.000
P-value			1.000

Table 11: Comparison of recurrence rates

Group	*n*	The number of recurrent cases	Recurrence rate (%)
Control group	17	2	11.76
Combination group	26	2	7.69
χ^2-value (χ^2 test)			0.000
P-value			1.000

All adverse reactions in both groups resolved spontaneously within three days without any special intervention. There was no statistically significant difference observed between the two groups (χ^2=0.000, *P*=1.000). See Table 10.

Comparison of recurrence rates

During the three-month follow-up period after treatment, recurrence was observed among responding patients in both groups. In the control group, 2 of the 17 patients who showed a significant response experienced recurrence, yielding a recurrence rate of 11.76%. In the combination therapy group, recurrence occurred in 2 of the 26 significant responders, corresponding to a recurrence rate of 7.69%. No statistically significant difference was found between the two groups (χ^2 = 0.000, P = 1.000). See Table 11.

DISCUSSION

Clinical efficacy and symptom improvement

Erosive OLP is one of the numerous subtypes of OLP. In addition to white lesions, the mucosa between the striae and surrounding the lesions may exhibit congestion, erosion and ulceration. Patients often suffer from significant pain, dysgeusia and other symptoms, which severely impact their daily lives (Stolte *et al.*, 2024). Moreover, prolonged non-healing of erosive OLP may increase the risk of malignant transformation, imposing significant psychological stress on patients (Offen and Allison, 2022). Clinically, long-term, standardized and comprehensive treatment is advocated. The treatment principles aim to alleviate pain, control lesion progression, promote erosion healing and reduce the potential for malignant transformation (Deng *et al.*, 2022). Therefore, to reduce patient suffering and treat the disease more effectively, there is an urgent need for safer and more efficient treatment methods needed.

This experiment investigated the clinical efficacy of combining cetylpyridinium chloride mouthwash with triamcinolone acetonide oral ointment in the treatment of patients with erosive OLP, demonstrating a significantly higher overall effective rate in the combination group than in the control group. Moreover, the combination therapy demonstrated superior performance in major outcome indicators such as pain improvement, promotion of mucosal lesion repair and reduction of erosion area. This suggests that the treatment regimen combining cetylpyridinium chloride mouthwash with triamcinolone acetonide exhibits more robust efficacy in clinical practice.

Mechanisms underlying enhanced therapeutic effects

From the perspective of disease treatment principles, triamcinolone acetonide, as a medium- to long-acting glucocorticoid, exerts its anti-inflammatory effects primarily by inhibiting arachidonic acid metabolism, thereby reducing the production of inflammatory mediators such as prostaglandins and leukotrienes. Simultaneously, it stabilizes lysosomal membranes, preventing the release of hydrolytic enzymes by inflammatory cells and thus exerts anti-inflammatory, anti-allergic and immunosuppressive effects (Fernandes *et al.*, 2022). However, long-term monotherapy with glucocorticoids may trigger a series of adverse reactions, such as oral mucosal atrophy, capillary dilation, secondary infections and has limited effects in regulating the oral microbiota structure (Wang *et al.*, 2020). The main component of cetylpyridinium chloride mouthwash is cetylpyridinium chloride, a cationic quaternary ammonium salt compound with significant broad-spectrum antibacterial activity that interferes with bacterial cell wall synthesis, thereby inhibiting bacterial growth and reproduction (Yang *et al.*, 2023). This property confers strong antibacterial capabilities against a variety of Gram-positive and Gram-negative bacteria, effectively inhibiting harmful bacterial growth and reproduction in the oral cavity, reducing sources of inflammation and thus providing a cleaner therapeutic environment for triamcinolone acetonide, enhancing its anti-inflammatory effects (Lv *et al.*, 2023; Zhu *et al.*, 2023). This synergistic effect contributes to improved overall treatment outcomes.

Impact on oral microbiota

Oral bacteria exist in two states: one as free-floating bacteria in flowing saliva and the other as attached bacteria colonizing on surfaces such as the oral mucosa, tooth surfaces and gingival crevices (Bloch *et al.*, 2024). Free-floating and attached bacteria are interconnected and influence each other to a certain extent. There is a relationship between bacteria in saliva and those on erosive wound surfaces, suggesting the necessity of studying salivary bacteria in erosive OLP. In terms of oral microbiota, the combination group exhibited lower detection rates of *Staphylococcus* and *Candida albicans* in the oral cavity after treatment. This indicates that cetylpyridinium chloride mouthwash indeed exerted its antibacterial properties, specifically reducing the number of potentially harmful bacteria (Brookes *et al.*, 2023). The balance of oral microbiota is crucial for maintaining the health of the oral mucosa. Under normal circumstances, various bacteria in the oral cavity mutually restrict and depend on each other, forming a stable microecological system (Hernandez-Cabanyero and Vonaesch, 2024; Sahingur *et al.*, 2024). When dysbiosis occurs, harmful bacteria may proliferate excessively, triggering inflammatory responses and exacerbating the condition of OLP. *Staphylococcus* and *Candida albicans* infections may stimulate immune responses in affected tissues, causing both inflammatory cell migration and mediator release. Such immunological reactions could worsen mucosal injury and facilitate erosive OLP initiation and advancement. Cetylpyridinium chloride mouthwash inhibits or kills bacteria by reducing bacterial surface tension, increasing cell membrane permeability and disrupting bacterial cell membrane structures, thereby reducing the detection of specific pathogens such as *Staphylococcus* and *Candida albicans* in the culture-based assay. This, in turn, alleviates inflammation and promotes the repair of the oral mucosa (Weber *et al.*, 2023).

Modulation of Th17/Treg balance and immune profile

In the immune system, Th17 and Treg cells are key T cell subsets involved in inflammation and immune regulation. Th17 cells mainly produce pro-inflammatory cytokines like IL-17 and TNF-α to drive inflammation. Conversely, Treg cells release anti-inflammatory cytokines such as IL-10 to regulate and suppress immune responses, ensuring immune system balance (Liu *et al.*, 2024). In patients with OLP, the Th17/Treg balance is often disrupted, manifesting as relatively hyperactive Th17 cell function, leading to persistent inflammation (Wu *et al.*, 2023). While the study confirms this imbalance in erosive OLP patients, the observed restoration of Th17/Treg balance following combination therapy should be interpreted within the constraints of a retrospective design. Rather than establishing novel pathways, the findings provide clinical support for the biological plausibility that microbial reduction may alleviate immune dysregulation. Moreover, research has shown that in oral epithelial cells of OLP patients, *Escherichia coli* substantially increases the proportion of Th17 cells via the TLR4/NF-κB pathway, worsening the Th17/Treg imbalance and affecting OLP's pathological process (Wang *et al.*, 2023). Similarly, reductions in *Staphylococcus* and *Candida albicans* in the cohort may indirectly lower Th17 activation, though causative links cannot be inferred from retrospective data. This study shows that combination therapy significantly lowers chemerin levels, the proportion of Th17 cells, the Th17/Treg ratio and inflammatory cytokines like IL-17 and TNF-α, while also raising the percentage of Treg cells and IL-10 levels. This suggests that the combination therapy regimen likely exerts dual antimicrobial and immunomodulatory effects, consistent with known mechanisms of cetylpyridinium chloride and triamcinolone acetonide (Ardizzoni *et al.*, 2018; Dey and Bishayi, 2017; Fantozzi *et al.*, 2019; Ma *et al.*, 2024). It is important to note that the immunology results, while consistent with prior experimental studies, are derived from a retrospective clinical cohort. Thus, they serve to confirm associations rather than elucidate new mechanisms. Future prospective and *in-vitro* studies are needed to dissect the precise causal relationships between oral microbiota shifts, Th17/Treg dynamics and clinical outcomes in OLP. Nevertheless, the convergence of microbial and immune improvements in the combination group supports the biological plausibility of targeting both axes in OLP management.

Improvement in oral health-related quality of life

The study results demonstrate that patients in the combination group exhibited more significant improvements in OHIP-14 scores, indicating that this treatment regimen has distinct advantages in enhancing oral health-related quality of life. As a common chronic oral mucosal disease, OLP often severely impacts patients' daily quality of life due to functional impairments such as oral pain and difficulty eating, which can even lead to psychological issues like social withdrawal (Daume, *et al*., 2020). Clinical observations have revealed that effective therapeutic interventions not only alleviate mucosal lesions but, more importantly, help patients restore normal oral function, improve their dietary status and consequently enhance their self-care abilities and confidence in social interactions. An ideal treatment approach should not only focus on curing the disease but also prioritize the overall health status and quality of life of the patient.

Clinical implications

The combined use of cetylpyridinium chloride mouthwash and triamcinolone acetonide in OLP treatment offers both operational convenience and proven therapeutic outcomes, making it feasible for application across different levels of medical institutions. Given its safety profile and ease of use, this combination could be integrated into initial management strategies for erosive OLP, particularly in outpatient or primary care settings. It may also serve as a step-up regimen for patients with inadequate response to

topical steroids alone, or as part of a multidisciplinary approach alongside regular monitoring and patient education. This study provides evidence-based support for clinical medication in oral mucosal diseases, offering significant guidance for optimizing the diagnostic and treatment protocols for OLP. In terms of mechanistic research, this study has unveiled the synergistic role of oral microbiota dysbiosis and immune imbalance in the pathogenesis of OLP, elucidating the regulatory effects of pharmacological interventions on these two critical aspects. This sets the direction for subsequent in-depth basic research. Future studies can further investigate the specific signaling pathways through which particular oral microbiota influence the immune system and explore how to precisely utilize microbiota modulation for immunotherapy. Additionally, based on the findings of this study, there is potential to explore and develop new oral microbiota regulators or immunomodulatory drugs, providing more treatment options for OLP.

While the antimicrobial properties of CPC and the anti-inflammatory effects of triamcinolone acetonide are well-established individually, their combined use in OLP represents a strategic integration of microbial and immunologic targeting (Bakhshi *et al.*, 2020; LeBel *et al.*, 2020). Previous studies have suggested adjunctive antimicrobial approaches in OLP, but few have systematically documented the concomitant modulation of oral microbiota and the Th17/Treg balance in a clinical cohort (Wang *et al.*, 2023; Wang *et al.*, 2025). The findings demonstrate that CPC not only reduces pathogenic bacteria such as *Staphylococcus* and *Candida albicans* but it is also associated with a significant rebalancing of Th17/Treg ratios and cytokine profiles. This supports the hypothesis that microbial dysbiosis directly contributes to Th17-driven inflammation in OLP and that its correction can augment the immunomodulatory effects of corticosteroids. Thus, this study provides clinical validation for a pathophysiologically grounded combined therapy, highlighting the potential of CPC as more than a mere antimicrobial agent but also an immunomodulatory adjunct in OLP management.

Study limitations

Despite the achievements of this study, several limitations exist. Firstly, regarding microbiological assessment, this study relied on culture-based methods to detect selected microorganisms. While informative for targeted pathogens, this approach does not capture the full taxonomic and functional diversity of the oral microbiome. Future studies utilizing 16S rRNA gene sequencing or metagenomic approaches would be valuable to comprehensively characterize microbial community shifts and elucidate ecological dynamics in OLP. Secondly, due to the retrospective study design, confounding factors were controlled for through baseline characteristic matching; however, it remains impossible to completely avoid the influence of selection bias and potential confounding variables. Thirdly, due to the limitations of a single-center design and a relatively small cohort (n=80), the statistical robustness and broader applicability of the results may be affected. Additionally, the follow-up period in this study was 3 months, which may be insufficient for observing the recurrence patterns of a chronic disease like OLP.

Future recommendations

Based on the limitations and findings of this study, future research should prioritize prospective, randomized, placebo-controlled trials with extended follow-up periods (6-12 months) to better evaluate long-term efficacy and recurrence. Multi-center collaborations and larger sample sizes are needed to enhance generalizability. Advanced sequencing methods should replace culture-based approaches to fully characterize oral microbiome dynamics. Mechanistic studies are warranted to elucidate how cetylpyridinium chloride influences Th17/Treg balance and immune signaling. Additionally, exploring biomarkers for personalized therapy and testing combinations with emerging treatments could further optimize OLP management and patient-centered outcomes.

CONCLUSION

In summary, this study provides evidence-based support for a combined antimicrobial-immunomodulatory strategy in managing erosive OLP. The regimen of cetylpyridinium chloride mouthwash combined with triamcinolone acetonide demonstrated superior clinical efficacy by simultaneously targeting two key pathological components: oral microbial dysbiosis (reducing pathogenic *Staphylococcus* and *Candida albicans*) and immune imbalance (restoring the Th17/Treg ratio and modulating pro-/anti-inflammatory cytokines). This dual action likely underlies the observed enhancements in mucosal healing, symptom relief and quality of life within the observed 4-week treatment and 3-month follow-up period. It provides important theoretical support and practical guidance for further optimizing the treatment strategies for OLP. However, when promoting and applying the findings of this study, it is also necessary to fully consider its limitations and continuously improve and validate its clinical value through subsequent, more in-depth and broader research. However, longer-term follow-up (e.g., 6–12 months) is recommended in future studies to better evaluate recurrence rates and sustained therapeutic effects.

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None

Authors' contributions

Lingshan He: Developed and planned the study, performed experiments and interpreted results. Edited and refined the manuscript with a focus on critical intellectual contributions; Quanqiang Zhong: Participated in

collecting, assessing and interpreting the data. Made significant contributions to date interpretation and manuscript preparation; Tianyi Li and Xinfeng Zhang: Provided substantial intellectual input during the drafting and revision of the manuscript.

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Data availability statement
The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval
The study protocol was reviewed and approved by the Ethics Committee of the First People's Hospital of Wuyi County, Zhejiang Province (Approval No. YZ: 20220625). All procedures were conducted in accordance with the ethical standards of the institutional research committee and the Helsinki Declaration and its subsequent amendments.

Conflict of interest
The authors declare that they have no conflicts of interest.

Consent to participate
A signed informed consent form was obtained from each participant.

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