

Original Article

Effects of topical vitamin C compound powder on healing time and pain relief in oral ulcers

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Abstract: Aims: To evaluate the clinical efficacy and safety of topical vitamin C compound powder in patients with oral ulcers, with a particular focus on its effects on ulcer healing time, pain relief, short-term clinical response, and patient-reported recovery outcomes. Methods: In this retrospective observational study, 300 patients diagnosed with oral ulcers were enrolled. They were divided according to routine clinical treatment regimens: 145 patients received local normal saline treatment alone (control group), and 155 patients received topical vitamin C compound powder combined with identical saline-based basic care (observation group). Primary endpoints included time to pain relief, burning relief, resumption of normal oral intake, complete healing, and complete healing rates at day 5 and day 7. Secondary endpoints comprised longitudinal symptom changes, overall clinical effectiveness, safety and tolerability, patient-reported outcomes, short-term ulcer recurrence, and hospital revisit rates. Multivariable logistic and Cox regression analyses were performed to identify independent prognostic factors for ulcer healing. Results: Compared with the control group, the observation group showed significantly shorter times to pain relief, burning relief, dietary recovery and complete ulcer healing (all $P < 0.001$), accompanied by elevated 5-day and 7-day complete healing rates and a lower proportion of unhealed lesions on day 7 (all $P < 0.001$). Although visual analogue scale (VAS) pain scores, burning sensation scores and eating interference scores declined progressively in both groups, the observation group exhibited superior symptom amelioration on day 3, 5, and 7 (all $P < 0.001$). The 7-day overall therapeutic effective rate was markedly higher in the observation group (89.0% vs. 62.8%, $P < 0.001$). Additionally, patients in the observation group reported higher treatment satisfaction, better quality-of-life improvement and stronger willingness to reuse the intervention (all $P < 0.001$). Multivariable regression verified that topical vitamin C compound powder treatment was an independent protective factor for 7-day complete ulcer healing (adjusted OR = 0.118; 95% CI: 0.048-0.289; $P < 0.001$) and accelerated wound healing (HR = 1.549; 95% CI: 1.302-1.775; $P < 0.001$). Conclusion: Topical vitamin C compound powder significantly accelerated oral ulcer healing, enhanced pain relief, and improved short-term patient-reported recovery outcomes, with favorable clinical safety and tolerability.

Keywords: Oral ulcers, topical vitamin C, compound powder, wound healing, pain relief

Introduction

Oral ulcers are one of the most common oral mucosal lesions, which lead to pain, difficulty eating, and decreased quality of life in general practice and dental clinics [1]. Most ulcers can heal on their own, but the burning pain, tenderness, and discomfort caused by eating, drinking, and speaking often prompt patients to actively seek treatment. In clinical practice, there are still many challenges in the treatment of recurrent aphthous ulcers and non-

malignant superficial oral ulcers: there is often a significant difference between the severity of ulcer symptoms and the size of the lesion, and the natural healing cycle fluctuates greatly [2-4]. Therefore, minimizing the duration of ulcers and maximizing pain relief are the core goals of oral ulcer treatment.

Currently, the mainstream treatment for oral ulcers is mainly symptomatic and supportive treatment [5]. Most treatment plans revolve around four main directions: anti-inflammatory,

analgesic, avoidance of secondary irritation, and promotion of mucosal repair. Commonly used drugs include topical corticosteroids, disinfectant and antiseptic agents, local anesthetics, protective pastes, and various mucosal repair agents [6, 7]. However, the efficacy of the above-mentioned treatments is not always satisfactory. Some drugs have too short analgesic duration, and some preparations cause local irritation and have a poor taste, which is not conducive to the repair of epithelial tissue. Furthermore, there is an urgent need in clinical practice for low-risk, low-cost, and easy-to-operate ulcer intervention programs that are suitable for use in outpatient and community settings.

Vitamins participate in multiple physiological processes such as collagen synthesis, tissue repair, and inflammation regulation, and are therefore regarded as highly promising adjuvant drugs for the treatment of mucosal wounds, attracting widespread attention [8]. From the perspective of mechanism of action, vitamin C can improve the wound microenvironment to accelerate ulcer healing, while relieving pain caused by mucosal damage [9]. Compound powders have unique advantages as drug delivery carriers, which can improve the adhesion of drugs to the ulcer surface, prolong the drug contact time, and isolate external factors from stimulating the ulcer wound. Although this theory has a reasonable basis, clinical evidence supporting the treatment of oral ulcers with topical vitamin C powder is very scarce, and there are no rigorously designed studies to evaluate its healing and analgesic effects.

Despite the theoretical advantages, high-quality clinical evidence validating the analgesic and healing-promoting efficacy of topical vitamin C compound powder remains insufficient. Given the above research gaps, this retrospective clinical study was conducted to systematically evaluate the clinical value of this topical preparation in oral ulcer management, so as to provide evidence for optimizing non-invasive oral ulcer treatment regimens.

Materials and methods

Study design

This retrospective observational study screened clinical records of 300 oral ulcer patients

admitted to the Central Medical District of Chinese PLA General Hospital from January 2023 to December 2024. Patients were grouped based on routine clinical treatment regimens: 145 cases received single normal saline care (control group), and 155 cases received topical vitamin C compound powder combined with identical saline care (observation group). The compound powder was composed of vitamin C tablets, vitamin B2 tablets and berberine tablets mixed at a 1:1:1 mass ratio, with no additional excipients added. Before administration, qualified tablets were separately ground into fine powder, blended homogeneously, and stored in sealed dry containers at room temperature. The dry powder was applied directly to the ulcer surface once per day. Given the dry-powder dosage form, pH value and in-vitro dissolution properties were not applicable for detection. All powder samples were sieved with standardized fine mesh screens to unify particle size, and the preparation procedure was strictly unified throughout the study to ensure reproducibility. This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of the Central Medical District of Chinese PLA General Hospital. Due to the retrospective nature and use of anonymized clinical data, the requirement for informed consent was waived.

Inclusion and exclusion criteria

Inclusion criteria: (1) Clinically diagnosed primary oral ulcer during the study period; (2) Complete baseline clinical characteristics, treatment regimen and follow-up information; (3) Receiving either local normal saline care or combined treatment with vitamin C compound powder plus normal saline; (4) Documented valid pain and healing outcome data.

Exclusion criteria: (1) Incomplete key clinical and follow-up data; (2) Unclear ulcer etiology and asymptomatic atypical oral lesions; (3) Poor treatment compliance or interrupted local medication; (4) Receiving other topical or systemic treatment during observation; (5) Complicated with severe secondary oral infections or other concomitant oral mucosal diseases interfering with outcome evaluation; (6) Uncontrolled severe systemic diseases affecting clinical assessment; (7) Malignant oral ulcers and traumatic ulcers requiring surgical intervention; (8) Lost to follow-up with unascertain-

tainable therapeutic outcomes. These criteria were set to unify the study population and eliminate confounding bias, ensuring the reliability of efficacy evaluation.

Data collection

A standardized case report form was used to collect demographic and clinical characteristics, ulcer-related parameters, symptom scores, laboratory biomarkers, safety data, and follow-up outcomes. Demographic and clinical variables included age, sex, body mass index (BMI), current ulcer episode duration, and relevant medical history.

Baseline ulcer-related indicators included ulcer number, maximum ulcer diameter, total ulcer area, ulcer depth score, peripheral erythema score, and surface exudation score. Spontaneous pain was assessed using a 10-point visual analogue scale (VAS), while burning sensation, eating interference, and speaking interference were evaluated using semi-quantitative scoring systems. Clinical and symptomatic assessments were performed at baseline, as well as on days 3, 5, and 7 after treatment initiation.

Peripheral venous blood samples were collected at baseline and on day 7 of treatment. Serum inflammatory biomarkers included interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and high-sensitivity C-reactive protein (hs-CRP). Detected growth factors included epidermal growth factor (EGF), transforming growth factor- β 1 (TGF- β 1), and vascular endothelial growth factor (VEGF). All biomarker levels were measured using enzyme-linked immunosorbent assay (ELISA) in accordance with standard experimental protocols.

Uniform quantitative criteria were predefined for key efficacy endpoints. Complete healing was defined as full re-epithelialization of the ulcer surface, complete pseudomembrane disappearance, no visible exudation, and complete resolution of peripheral erythema. Pain relief and burning relief were defined as a minimum 30% reduction in respective baseline scores. Pain-free status was defined as a VAS pain score of 0. Resumption of normal oral intake was defined as an eating interference score of 0 or 1. Predefined adverse events, patient-reported outcomes, short-term ulcer re-

currence, and hospital return visits were fully recorded during the follow-up period.

Outcome measures

The primary endpoints were time to pain relief, time to burning relief, time to resumption of normal oral intake, and time to complete healing. The rates of complete healing at 5 and 7 days after treatment were also evaluated as primary efficacy outcomes.

Secondary endpoints included longitudinal changes in VAS pain score, burning sensation score, and eating interference score; residual unhealed lesions on day 7, the proportion of patients achieving pain-free status by day 5, rescue analgesic consumption, and persistent eating interference on day 7.

Overall clinical efficacy was assessed on day 7 after treatment. Efficacy was categorized into four grades: markedly effective, effective, improved, and ineffective. The total clinical effective rate was calculated based on this grading standard. Safety outcomes included the incidence of predefined adverse events and overall treatment tolerability. Patient-reported outcomes comprised treatment satisfaction, quality-of-life improvement, willingness to reuse the treatment, subjective symptom recovery, sleep improvement, and functional recovery of eating and speaking abilities. Changes in serum inflammatory cytokines and growth factors were considered exploratory biological outcomes. Ulcer recurrence and return visits within 14 days were recorded as short-term follow-up outcomes after treatment.

Statistical analysis

Normally distributed data were expressed as mean $\pm$ standard deviation, and non-normally distributed data were reported as median (interquartile range). Categorical variables were presented as case number (percentage). Between-group baseline comparisons adopted independent samples t-test or Mann-Whitney U test for continuous variables, and chi-square test or Fischer's exact test for categorical variables. Repeated-measures variance analysis was applied to analyze longitudinal symptomatic changes; post-hoc pairwise comparison with multiple testing correction was conducted once significant overall inter-group effects

Table 1. Baseline demographics after propensity score matching

Variable	Control group (n = 145)	Observation group (n = 155)	Statistic	P value
Propensity score	0.49 ± 0.12	0.51 ± 0.12	t = -1.387	0.166
Age, years	40.72 ± 14.38	39.00 ± 12.89	t = 1.095	0.275
Male sex, n (%)	71 (49.0)	79 (51.0)	$\chi^2 = 0.120$	0.729
Body mass index, kg/m ²	23.63 ± 3.41	23.41 ± 3.43	t = 0.560	0.576
Disease duration before presentation, days	3.91 ± 1.56	3.98 ± 1.79	t = -0.362	0.718
Recurrent history of oral ulcers, n (%)	63 (43.4)	73 (47.1)	$\chi^2 = 0.402$	0.526
Smoking history, n (%)	29 (20.0)	27 (17.4)	$\chi^2 = 0.329$	0.566
Alcohol use, n (%)	34 (23.4)	39 (25.2)	$\chi^2 = 0.119$	0.730
Diabetes mellitus, n (%)	18 (12.4)	16 (10.3)	$\chi^2 = 0.326$	0.568
Hypertension, n (%)	26 (17.9)	24 (15.5)	$\chi^2 = 0.323$	0.570
Recent upper respiratory infection, n (%)	21 (14.5)	25 (16.1)	$\chi^2 = 0.156$	0.692

were observed. Time-to-event outcomes were analyzed using Kaplan-Meier survival analysis, and between-group differences were compared using log-rank test. Binary therapeutic outcomes were compared using chi-square test or Fisher's exact test as appropriate.

Prespecified subgroup analysis was performed stratified by ulcer number, lesion diameter, baseline pain severity, disease course and recurrence history. Multivariable logistic regression was used to screen independent predictors for 7-day complete healing, with adjusted odds ratio (OR) and 95% confidence interval (CI) calculated. Cox proportional hazards (PH) regression model was adopted to identify factors affecting healing speed, and hazard ratio (HR) with 95% CI was reported. Covariates enrolled in regression models included treatment regimen, age, sex, ulcer number, maximum lesion diameter, pre-treatment disease course, recurrent ulcer history, baseline pain severity, diabetes mellitus and early treatment response. All statistical tests were two-tailed, and $P < 0.05$ was defined as the threshold of statistical significance.

Results

Baseline demographic and general clinical characteristics

The baseline demographic and overall clinical profiles were well-balanced between the two groups, with no significant inter-group differences in age ($P = 0.275$), sex distribution ($P = 0.729$), body mass index ($P = 0.576$), or ulcer

duration at presentation ($P = 0.718$). Relevant medical history and other routine clinical characteristics were also comparable (all $P > 0.05$) (**Table 1**).

Baseline ulcer-related clinical characteristics

No statistically significant between-group differences were observed in ulcer number ($P = 0.337$), maximum ulcer diameter ($P = 0.723$), total ulcer area ($P = 0.568$), ulcer depth score ($P = 0.729$), peripheral erythema score ($P = 0.804$) or surface exudation score ($P = 0.907$). Baseline subjective symptomatic scores, including VAS pain score, burning sensation score, eating and speaking interference scores, also showed no inter-group discrepancy (all $P > 0.05$) (**Table 2**).

Primary healing outcomes

The observation group achieved significantly shortened time to pain relief, burning remission, dietary recovery and complete ulcer healing (all $P < 0.001$). Meanwhile, the observation group had higher 5-day and 7-day complete healing rates, lower residual unhealed lesion rate on day 7, higher 5-day pain-free rate, less rescue analgesic consumption and lower incidence of persistent eating dysfunction on day 7 (all $P < 0.001$) (**Table 3**).

Dynamic changes in pain-related outcomes over time

As illustrated in **Figure 1**, pain-related symptoms improved continuously in both groups after treatment, yet the observation group pre-

Table 2. Baseline ulcer-related clinical characteristics

Variable	Control group (n = 145)	Observation group (n = 155)	Statistic	P value
Number of ulcers	2.24 ± 0.70	2.37 ± 1.58	t = -0.886	0.337
Maximum ulcer diameter, mm	5.70 ± 1.95	5.79 ± 2.21	t = -0.355	0.723
Total ulcer area, mm ²	25.02 ± 10.84	25.68 ± 8.97	t = -0.572	0.568
Ulcer depth score	2.14 ± 0.75	2.19 ± 1.79	t = -0.347	0.729
Peripheral erythema score	2.19 ± 0.75	2.15 ± 1.33	t = 0.249	0.804
Surface exudation score	1.68 ± 0.56	1.69 ± 0.55	t = -0.117	0.907
Baseline pain VAS (0-10)	7.11 ± 0.99	7.15 ± 1.03	t = -0.381	0.703
Burning sensation score	6.88 ± 1.57	6.79 ± 1.49	t = 0.466	0.641
Eating interference score	6.06 ± 1.58	6.13 ± 1.75	t = -0.347	0.729
Speaking interference score	4.70 ± 1.56	4.77 ± 1.82	t = -0.360	0.719

Table 3. Primary healing outcomes

Outcome	Control group (n = 145)	Observation group (n = 155)	Statistic	P value
Time to pain relief, days	4.82 ± 1.53	2.96 ± 1.26	t = 11.525	< 0.001
Time to burning relief, days	4.38 ± 1.44	2.77 ± 1.24	t = 10.403	< 0.001
Time to oral intake normalization, days	4.92 ± 1.80	3.46 ± 1.33	t = 8.060	< 0.001
Time to complete healing, days	8.07 ± 2.29	5.77 ± 1.62	t = 10.083	< 0.001
Healing within 5 days, n (%)	21 (14.5)	76 (49.0)	$\chi^2 = 40.873$	< 0.001
Healing within 7 days, n (%)	69 (47.6)	130 (83.9)	$\chi^2 = 44.167$	< 0.001
Residual ulcer at day 7, n (%)	76 (52.4)	25 (16.1)	$\chi^2 = 44.167$	< 0.001
Pain-free status by day 5, n (%)	44 (30.3)	107 (69.0)	$\chi^2 = 44.854$	< 0.001
Need for rescue analgesic use, n (%)	38 (26.2)	17 (11.0)	$\chi^2 = 11.620$	0.001
Persistent eating difficulty at day 7, n (%)	33 (22.8)	9 (5.8)	$\chi^2 = 17.881$	< 0.001

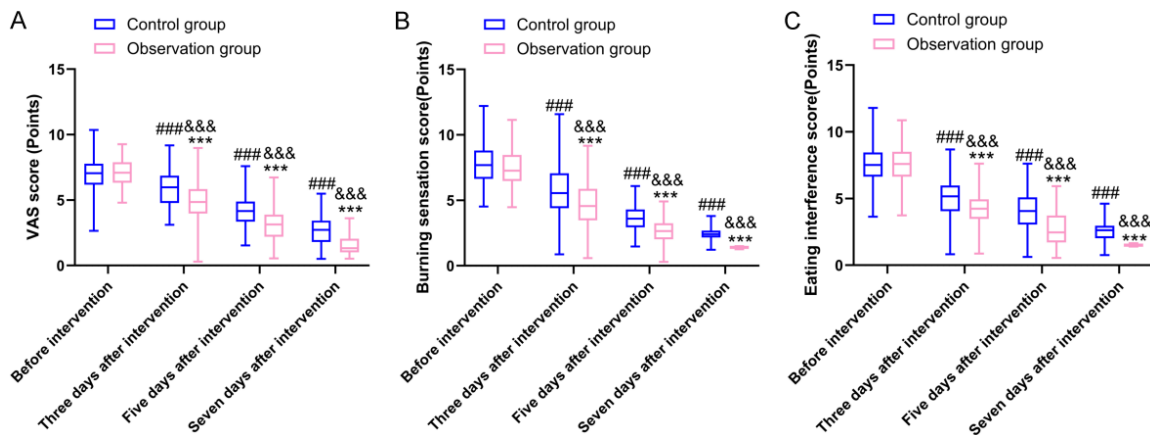


Figure 1. Dynamic changes in pain-related outcomes over time. (A) Changes in visual analogue scale (VAS) pain scores, (B) burning sensation scores, and (C) eating interference scores. Compare to the control group, ***P < 0.001. Compare to the control group before intervention, ###P < 0.001. Compare to the intervention group before intervention, &&&P < 0.001.

sented faster and more substantial symptomatic amelioration. Both groups showed remarkable declines in VAS pain score, burning sen-

sation score and eating interference score at day 3, day 5 and day 7 versus baseline (all P < 0.001). Nevertheless, the observation

Table 4. Safety and tolerability outcomes

Adverse event/tolerability parameter	Control group (n = 145)	Observation group (n = 155)	Statistic	P value
Any local discomfort, n (%)	9 (6.2)	15 (9.7)	$\chi^2 = 1.226$	0.268
Transient stinging sensation, n (%)	5 (3.4)	11 (7.1)	$\chi^2 = 1.975$	0.160
Bitter taste complaint, n (%)	0 (0.0)	13 (8.4)	$\chi^2 = 12.712$	< 0.001
Mild mucosal dryness, n (%)	6 (4.1)	9 (5.8)	$\chi^2 = 0.439$	0.508
Mild nausea after application, n (%)	1 (0.7)	4 (2.6)	$\chi^2 = 1.635$	0.201
Allergic reaction, n (%)	0 (0.0)	1 (0.6)	$\chi^2 = 0.939$	0.333
Secondary infection, n (%)	4 (2.8)	2 (1.3)	$\chi^2 = 0.824$	0.364
Treatment discontinuation, n (%)	2 (1.4)	3 (1.9)	$\chi^2 = 0.141$	0.707
Good treatment tolerability, n (%)	131 (90.3)	137 (88.4)	$\chi^2 = 0.301$	0.583

Table 5. Patient-reported outcomes and short-term recurrence

Outcome	Control group (n = 145)	Observation group (n = 155)	Statistic	P value
Patient satisfaction score (0-10)	6.83 ± 1.60	8.55 ± 1.15	t = -10.764	< 0.001
Willingness to reuse same treatment, n (%)	94 (64.8)	135 (87.1)	$\chi^2 = 20.555$	< 0.001
Perceived rapid pain relief, n (%)	51 (35.2)	118 (76.1)	$\chi^2 = 51.087$	< 0.001
Perceived faster healing, n (%)	58 (40.0)	126 (81.3)	$\chi^2 = 53.857$	< 0.001
Sleep improvement by day 5, n (%)	63 (43.4)	119 (76.8)	$\chi^2 = 34.868$	< 0.001
Normal diet resumed by day 5, n (%)	56 (38.6)	121 (78.1)	$\chi^2 = 48.184$	< 0.001
Speaking discomfort resolved by day 5, n (%)	61 (42.1)	123 (79.4)	$\chi^2 = 43.917$	< 0.001
Overall quality-of-life improvement score	6.97 ± 1.61	7.79 ± 1.24	t = -5.008	< 0.001
Recurrence within 14 days, n (%)	19 (13.1)	11 (7.1)	$\chi^2 = 3.003$	0.083
Need for return visit within 14 days, n (%)	23 (15.9)	10 (6.5)	$\chi^2 = 6.777$	0.009

group maintained significantly lower symptomatic scores at all post-treatment timepoints (all $P < 0.001$), and the inter-group efficacy gap widened with treatment duration, indicating sustained therapeutic advantages of topical vitamin C compound powder rather than transient early symptomatic relief.

Safety and tolerability outcomes

Most adverse event indicators were comparable between the two groups, including local discomfort ($P = 0.268$), transient stinging sensation ($P = 0.160$), mild mucosal dryness ($P = 0.508$), post-application nausea ($P = 0.201$), allergic reaction ($P = 0.333$), secondary oral infection ($P = 0.364$) and treatment discontinuation rate ($P = 0.707$). Overall treatment tolerability was similar across groups ($P = 0.583$). The only statistically different adverse event was increased bitter taste complaint in the observation group ($P < 0.001$). Notably, this taste-related discomfort did not elevate treatment discontinuation rate or trigger other clinically adverse outcomes (Table 4).

Patient-reported outcomes and short-term recurrence

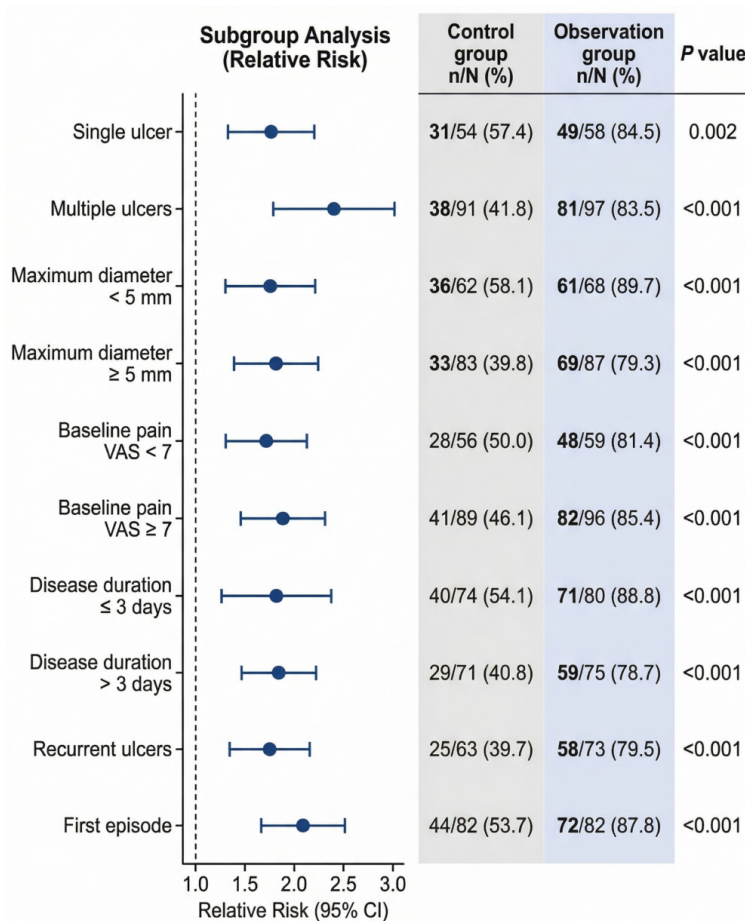
Patients in the observation group reported higher treatment satisfaction, better quality-of-life improvement and stronger re-treatment willingness (all $P < 0.001$). They also perceived rapid pain relief and ulcer healing, accompanied by superior functional rehabilitation, including improved sleep quality, early dietary recovery and relieved phonation discomfort (all $P < 0.001$). Although the 14-day ulcer recurrence rate showed a declining trend in the observation group, the difference failed to reach statistical significance ($P = 0.083$); the 14-day hospital revisit rate was markedly reduced in the observation group ($P = 0.009$) (Table 5).

Overall clinical effectiveness at seven days after intervention

The proportion of patients achieving markedly effective and effective outcomes was higher in

Table 6. Overall clinical effectiveness at seven days after intervention

Outcome category	Observation group (n = 155)	Control group (n = 145)	χ^2 value	P value
Markedly effective, n (%)	93 (60.0)	39 (26.9)	41.80	< 0.001
Effective, n (%)	45 (29.0)	52 (35.9)		
Improved, n (%)	11 (7.1)	31 (21.4)		
Ineffective, n (%)	6 (3.9)	23 (15.9)		
Total effective rate, n (%)	138 (89.0)	91 (62.8)	27.19	< 0.001


Figure 2. Stratified analysis of complete healing within 7 days.

the observation group, whereas the proportions of improved and ineffective cases were lower. The 7-day total therapeutic effective rate of the observation group was significantly higher than that of the control group (89.0% vs. 62.8%, $P < 0.001$) (Table 6).

Stratified analysis of complete healing within 7 days

Consistent treatment efficacy was verified across all clinical subgroups. Specifically, the 7-day healing rate of the observation group was

superior to the control group in patients with single ulcer (84.5% vs. 57.4%, $P = 0.002$) and multiple ulcers (83.5% vs. 41.8%, $P < 0.001$). The therapeutic advantage existed regardless of lesion size, including ulcers with maximum diameter < 5 mm (89.7% vs. 58.1%, $P < 0.001$) and ≥ 5 mm (79.3% vs. 39.8%, $P < 0.001$). Similarly, favorable healing outcomes were observed in patients with mild (VAS < 7) and severe baseline pain (VAS ≥ 7), short (≤ 3 days) and long (> 3 days) pre-treatment disease course, as well as first-episode and recurrent ulcer patients (all $P < 0.001$) (Figure 2).

Changes in serum inflammatory cytokines and growth factors

Baseline serum levels of inflammatory cytokines (IL-6, TNF- α , IL-1 β , hs-CRP) and repair-related growth factors (EGF, TGF- β 1, VEGF) were equivalent between groups

(all $P > 0.05$). On post-treatment day 7, both groups presented ameliorated systemic inflammation and activated tissue repair, while the observation group obtained more significant biomarker changes. Specifically, pro-inflammatory cytokines decreased sharply in both groups, with lower post-treatment levels detected in the observation group (all $P < 0.001$). By contrast, serum EGF, TGF- β 1 and VEGF levels increased after treatment, and the observation group showed remarkably higher growth factor concentrations (all $P < 0.001$) (Table 7).

Table 7. Changes in serum inflammatory cytokines and growth factors before and 7 days after intervention in the control and observation groups

Outcome	Time	Control group (n = 145)	Observation group (n = 155)	Statistic	P value
IL-6 (pg/mL)	Before intervention	28.06 ± 7.45	28.54 ± 7.32	-0.570	0.569
	Seven days after intervention	17.92 ± 5.52	12.19 ± 4.06	10.273	< 0.001
TNF-α (pg/mL)	Before intervention	31.50 ± 7.38	32.20 ± 7.29	-0.824	0.410
	Seven days after intervention	21.54 ± 5.23	13.31 ± 5.05	13.862	< 0.001
IL-1β (pg/mL)	Before intervention	19.51 ± 4.76	19.73 ± 5.04	-0.394	0.694
	Seven days after intervention	12.80 ± 4.15	7.78 ± 3.32	11.595	< 0.001
hs-CRP (mg/L)	Before intervention	6.13 ± 1.83	6.07 ± 1.89	0.275	0.784
	Seven days after intervention	3.89 ± 1.26	3.10 ± 1.66	4.649	< 0.001
EGF (pg/mL)	Before intervention	85.07 ± 18.36	87.01 ± 16.94	-0.954	0.341
	Seven days after intervention	102.60 ± 22.61	138.26 ± 24.59	-13.048	< 0.001
TGF-β1 (pg/mL)	Before intervention	42.19 ± 9.80	40.38 ± 9.97	1.577	0.116
	Seven days after intervention	58.65 ± 12.32	78.31 ± 16.52	-11.619	< 0.001
VEGF (pg/mL)	Before intervention	114.66 ± 23.54	113.83 ± 22.29	0.315	0.753
	Seven days after intervention	128.42 ± 23.70	162.46 ± 29.70	-10.928	< 0.001

Table 8. Multivariable logistic regression for complete healing by day 7

Predictor	Coding/unit	Adjusted OR	95% CI	β coefficient	P value
Observation-group treatment	Yes vs no	0.118	0.048-0.289	2.141	< 0.001
Number of ulcers	Per 1-lesion increase	0.897	0.851-0.945	-0.109	< 0.001
Maximum ulcer diameter	Per 1-mm increase	0.112	0.050-0.249	-2.192	< 0.001
Disease duration before treatment	Per 1-day increase	3.125	1.362-4.173	-1.140	0.007
Early pain reduction at day 3 ≥ 30%	Yes vs no	1.549	1.302-1.775	0.438	< 0.001

Multivariable logistic regression for 7-day complete healing

Multivariable logistic regression demonstrated that topical vitamin C compound powder treatment was an independent protective factor for 7-day complete ulcer healing (adjusted OR = 0.118; 95% CI: 0.048-0.289; $P < 0.001$). Early ≥ 30% pain reduction on day 3 also independently predicted favorable healing outcomes (adjusted OR = 1.549; 95% CI: 1.302-1.775; $P < 0.001$). Conversely, increased ulcer number (adjusted OR = 0.897; 95% CI: 0.851-0.945; $P < 0.001$), larger maximum lesion diameter (adjusted OR = 0.112; 95% CI: 0.050-0.249; $P < 0.001$) and prolonged pre-treatment disease course (adjusted OR = 3.125; 95% CI: 1.362-4.173; $P = 0.007$) were independent risk factors for delayed healing. Age, sex, recurrent ulcer history, baseline pain severity and diabetes mellitus exerted no inde-

pendent impact on 7-day healing (all $P > 0.05$) (Table 8).

Cox proportional hazards model for time to complete healing

Multivariable Cox regression validated that topical vitamin C compound powder independently shortened ulcer healing time (HR = 2.08; 95% CI: 1.62-2.67; $P < 0.001$). Greater baseline ulcer burden delayed healing, including higher ulcer number (HR = 0.87; 95% CI: 0.76-0.99; $P = 0.041$), larger lesion diameter (HR = 0.84; 95% CI: 0.78-0.90; $P < 0.001$) and longer pre-treatment course (HR = 0.90; 95% CI: 0.82-0.99; $P = 0.033$). Age, male sex, recurrent ulcer history, baseline pain VAS score and diabetes mellitus showed no significant correlation with healing time (all $P > 0.05$). Notably, ≥ 25% ulcer area shrinkage on day 3 was a significant favorable predictor for sub-

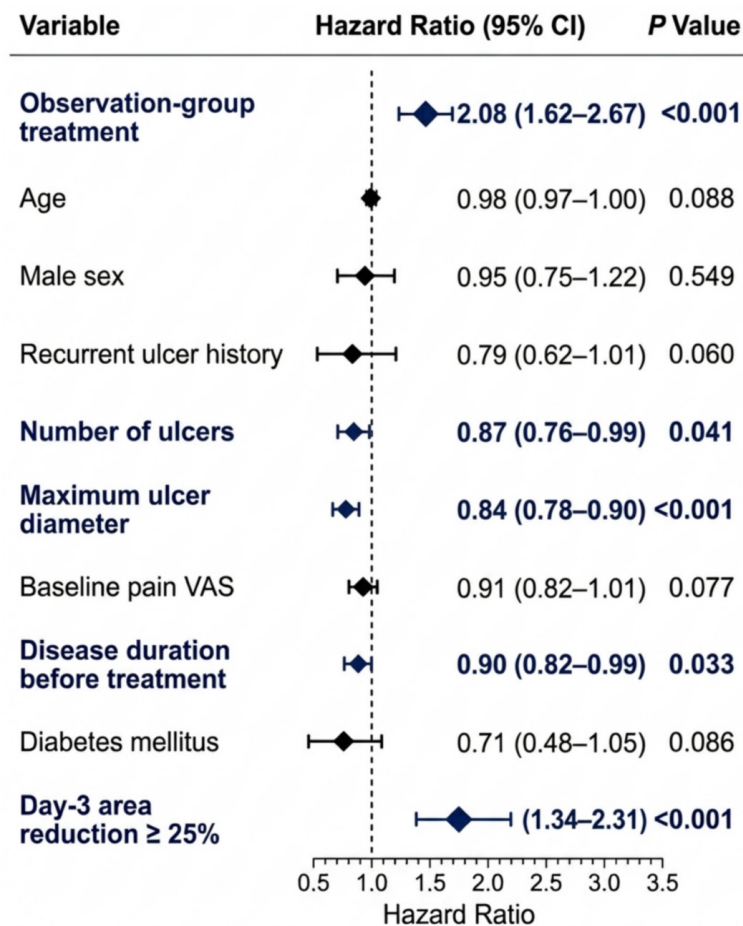


Figure 3. Cox proportional hazards model for time to complete healing.

sequent complete healing (95% CI: 1.34–2.31; $P < 0.001$) (Figure 3).

Discussion

The present retrospective observational study found that topical vitamin C compound powder combined with routine saline care yields faster ulcer healing and superior symptomatic relief compared with single saline treatment for oral ulcers. The observation group showed shorter times to pain relief, burning relief, dietary recovery and complete ulcer healing, as well as improved short-term patient-reported recovery and reduced hospital revisit rates. These therapeutic advantages remained stable across prespecified clinical subgroups. Moreover, multivariable logistic regression and Cox proportional hazard analyses indicated that topical vitamin C compound powder treatment was an independent protective factor for 7-day complete ulcer healing and shortened overall heal-

ing time. By comprehensively analyzing objective healing indicators, symptomatic scores, functional rehabilitation indexes and patient-reported outcomes, this study systematically evaluated the short-term clinical efficacy of topical vitamin C compound powder in oral ulcer treatment.

Topical vitamin C compound powder improves fundamental ulcer healing rather than merely relieving superficial pain. Clinical studies on topical treatment for recurrent aphthous stomatitis and minor oral ulcers have reported inconsistent efficacy, as therapeutic outcomes vary greatly by active ingredients, administration frequency and lesion severity [10, 11]. Different from conventional symptomatic treatments, the intervention in this study achieved reliable 5-day and 7-day ulcer healing efficacy based on sustained pain relief. The therapeutic mechanism relies on the biological function of vitamin C in promoting collagen synthesis

and extracellular matrix repair, as well as inhibiting excessive oxidative stress, which is essential for oral mucosal epithelial regeneration [12–14]. The compound powder can activate local mucosal healing pathways and optimize the ulcer microenvironment to facilitate lesion repair during the active inflammatory stage of oral ulcers. This treatment effectively improves the quality of life of patients, especially those with severe eating and phonation dysfunction caused by oral ulcers.

This intervention enables rapid and sustained relief of ulcer-related pain symptoms. Current clinical consensus confirms that pain relief is the primary therapeutic goal for oral ulcers. Ulcer pain severely impairs patients' dietary intake, verbal communication, sleep quality and overall quality of life [15–17]. However, most traditional topical agents only provide transient superficial analgesia and cannot achieve long-term symptomatic improvement.

In this study, patients in the observation group showed faster and more significant declines in pain score, burning sensation scores and eating interference scores at all post-treatment follow-up timepoints. This consistent inter-group difference indicates that the intervention can induce durable improvements in ulcer lesions and marginal microenvironments. We hypothesize that the compound powder inhibits local inflammatory amplification, reduces nociceptor sensitivity and accelerates epithelialization. The sustained mucosal healing further eliminates persistent pain in ulcer lesions and surrounding tissues [15]. Early symptomatic improvement is a robust predictive marker for final ulcer healing outcomes. However, single analgesic treatments that fail to target underlying inflammatory and repair disorders cannot effectively promote ulcer healing.

Subgroup analysis verified the stable therapeutic effect of vitamin C compound powder across diverse oral ulcer clinical phenotypes. Earlier studies have shown that topical treatments often have reduced efficacy for multiple, large, long-course and severe oral ulcers [18-20]. Nevertheless, the present study found that the intervention yielded consistent positive outcomes regardless of ulcer number, lesion size, symptom severity, disease duration and recurrence history. This indicates that the therapeutic effect is not limited to patients with mild ulcers, and all oral ulcer patients can benefit from this treatment. The core mechanism is that the compound powder targets the common pathological basis of oral ulcers, including local inflammatory response and mucosal repair dysfunction, and can regulate lesion microenvironments independent of baseline lesion burden. Although the treatment remained effective for high-burden ulcers, such patients required closer clinical monitoring and rational prognostic expectation due to their inherently slow repair progress.

Multivariable regression analysis confirmed that topical vitamin C compound powder treatment was an independent predictor of 7-day complete healing and shortened healing time, excluding the interference of baseline population differences and subjective reporting bias. Consistent with previous findings, increased ulcer number, larger maximum lesion diameter and prolonged pre-treatment disease course

were independent risk factors for delayed mucosal healing [21]. Early treatment response indicators, including $\geq 30\%$ pain reduction and $\geq 25\%$ ulcer area shrinkage on day 3, were strongly correlated with favorable final healing outcomes. Early symptomatic and morphological improvement verified that the intervention exerts dual effects of anti-inflammation and mucosal repair throughout the healing process. The rapid early pain relief is mainly attributed to effective local inflammatory control and accelerated epithelial repair [22]. These results highlight the necessity of early efficacy evaluation in oral ulcer treatment. Patients without obvious early improvement may have poor treatment response, requiring timely clinical re-evaluation, confirmation of treatment adherence and adjustment of individualized treatment regimens.

The intervention exhibited satisfactory safety and patient tolerability with no increased incidence of severe adverse events, treatment intolerance or local complications. Safety evaluation is critical for oral topical preparations, as mucosal irritation and poor taste will reduce patient adherence and offset symptomatic efficacy. In this study, bitter taste was the only adverse event with a significantly higher incidence in the observation group, which is biologically reasonable due to the inherent taste characteristics of the compound components. Importantly, this mild sensory discomfort did not reduce overall treatment tolerability or cause treatment discontinuation. This finding suggests that future formulation optimization can adopt targeted taste-masking technology to improve patient experience and treatment adherence without compromising therapeutic efficacy.

Beyond local symptomatic improvement, topical vitamin C compound powder also regulates systemic inflammatory and repair-related biological pathways, as evidenced by significant changes in peripheral serum biomarkers. The observation group showed significant reductions in serum pro-inflammatory factors including IL-6, TNF- α , IL-1 β , and hs-CRP, as well as elevated levels of repair-related growth factors including EGF, TGF- β 1, and VEGF on day 7 after treatment. Oxidative stress and persistent inflammatory amplification are key drivers of delayed oral mucosal healing [23, 24]. Vi-

tamin C can maintain redox homeostasis, inhibit NF- κ B-mediated pro-inflammatory signaling, and modulate macrophage polarization to alleviate systemic inflammation. Upregulated TGF- β 1 and VEGF promote extracellular matrix remodeling and angiogenesis, while EGF facilitates epithelial proliferation and re-epithelialization, jointly activating mucosal repair cascades [25]. Although peripheral serum biomarkers cannot fully reflect local microenvironmental changes of ulcer lesions, they objectively mirror the resolution of local inflammation and activation of regenerative repair. These molecular findings provide biological evidence for the clinical efficacy of the intervention and offer new directions for future in-depth research on mucosal proteomics, transcriptomics and microbiome characteristics of oral ulcer repair.

This study has several limitations. First, the short 14-day follow-up period only evaluated short-term therapeutic outcomes and failed to observe long-term ulcer recurrence rules, which explains the insignificant inter-group difference in short-term recurrence rate. Second, although multivariable analysis was adopted to control confounding bias, unmeasured factors such as individual dietary habits, nutritional status and immune level may still affect ulcer healing outcomes. Third, partial subjective symptomatic endpoints are susceptible to patient expectation and reporting bias. Fourth, this study did not stratify ulcer subtypes, etiological factors and systemic predispositions, which limits the generalized applicability of the research conclusions. Fifth, this study lacked targeted observation of rare adverse events due to its retrospective design. Finally, the biomarker detection in peripheral blood could not provide direct tissue-level evidence, and further histological and microbiological verification is needed to clarify the precise therapeutic mechanism of the compound powder.

Future research can develop mucoadhesive sustained-release carriers such as bioadhesive hydrogel films and in-situ gel matrices, combined with taste-masking and antioxidant stabilization technologies to prolong lesion retention time and improve treatment adherence. Meanwhile, individualized stratified treatment strategies should be established based on baseline lesion burden, symptom severity, re-

currence history and 3-day early treatment response to realize adaptive precise intervention. Furthermore, oral ulcer management should shift from episodic symptomatic treatment to standardized long-term prevention, with unified follow-up protocols and early intervention mechanisms to reduce ulcer recurrence. The integrated model of formulation optimization, precise stratification and standardized follow-up can transform empirical compound medication into a scalable and standardized intervention suitable for primary and specialized oral clinical settings.

In conclusion, topical vitamin C compound powder effectively relieves oral ulcer symptoms, accelerates mucosal healing, improves short-term clinical efficacy and patient-reported rehabilitation outcomes, with favorable safety and tolerability. Its therapeutic advantages are stable across diverse clinical subgroups and serve as an independent favorable prognostic factor for ulcer healing. This low-cost and convenient compound preparation is a reliable alternative treatment for oral ulcers, and early treatment response has potential prognostic value for final healing. Large-sample, long-term prospective studies are required to further verify its efficacy in reducing long-term ulcer recurrence and disease burden.

Disclosure of conflict of interest

None.

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