

Original Article

5-ALA-PDT combined with oral Kangfuxin solution improves HR-HPV outcomes, vaginal microecology and quality of life in patients with HPV-positive cervical erosion

Yake Gao^{1*}, Mei Qiao^{2*}, Jinfeng Guo³, Suping Yu⁴, Yu Gao¹, Hongna Xiao¹

¹Department of Traditional Chinese Medicine, Fourth Hospital, Shijiazhuang 050000, Hebei, China; ²Department of Obstetrics, Shijiazhuang Fourth Hospital, Shijiazhuang 050000, Hebei, China; ³Department of Obstetrics and Gynecology, Zhengding County Hospital of Traditional Chinese Medicine, Shijiazhuang 050800, Hebei, China; ⁴Department of Gynecology, Lincheng County People's Hospital, Xingtai 054000, Hebei, China. *Equal contributors.

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Abstract: Objective: To evaluate the efficacy, safety, and effects on related indicators of 5-aminolevulinic acid-mediated photodynamic therapy (5-ALA-PDT) combined with oral Kangfuxin liquid in patients with human papillomavirus (HPV)-positive cervical erosion. Methods: Patients admitted retrospectively from January 2022 to December 2024 were included. A total of 314 patients were initially screened, and 32 were excluded, leaving an original cohort of 282 patients (129 in the observation group and 153 in the control group). After propensity score matching (PSM) at a 1:1 ratio, 226 patients were included (113 in each group). This study compared clinical efficacy, cervical erosion grading, high-risk human papillomavirus (HR-HPV) seroconversion and re-seroconversion, gut microbiota, inflammatory factors, and scores on the 36-Item Short Form Health Survey (SF-36). Adverse reactions were also recorded, and multivariate logistic regression was performed. Results: The total effective rate was 96.46% in the observation group and 80.53% in the control group ($P < 0.001$); the improvement in erosion grading was more significant ($P < 0.001$). The HR-HPV seroconversion rates at 3 months were 80.5% and 63.7% ($P = 0.004$), and the re-seroconversion rates at 6 months were 7.7% and 26.4% ($P = 0.001$). After treatment, the vaginal pH was 4.25 ± 0.21 and 4.39 ± 0.30 ($P < 0.001$), and the proportion of vaginal cleanliness grades I-II increased from 30.97% to 97.35% ($P < 0.001$). Interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and C-reactive protein (CRP) levels all decreased, with even lower levels in the observation group (all $P < 0.001$); SF-36-related dimensions increased, with greater improvement in the observation group (all $P < 0.001$). Conclusion: Combining 5-ALA-PDT with oral Kangfuxin liquid can improve clinical efficacy and HR-HPV seroconversion rate, reduce recurrence, and improve microecology, inflammation, and quality of life, with comparable safety.

Keywords: Photodynamic therapy, Kangfuxin solution, human papillomavirus, cervical erosion, clinical efficacy

Introduction

Cervical erosion in modern gynecology often corresponds to cervical columnar epithelial ectopia, and is generally a benign appearance change. However, when accompanied by chronic cervicitis or vaginal microecological imbalance, patients often experience symptoms such as abnormal vaginal discharge, odor, and contact bleeding, affecting their quality of life and leading to repeated visits to the doctor [1, 2]. Meanwhile, human papillomavirus (HPV)

infection is highly prevalent among women, and persistent infection with high-risk HPV (HR-HPV) is a prerequisite for the development of cervical intraepithelial neoplasia and cervical cancer. Blocking persistent infection remains a key focus of prevention and control [3]. Although most HPV infections can clear spontaneously, in the context of persistent inflammation, damaged epithelial barrier, and local immune imbalance, the virus is more likely to persist and relapse or become chronic [4-6]. Therefore, for patients with HPV-positive cervical erosion, the

treatment goal should not be limited to local appearance improvement, but should also consider virus clearance, mucosal repair, and microecological reconstruction to reduce the risk of relapse and improve the overall benefit for patients. 5-aminolevulinic acid-mediated photodynamic therapy (5-ALA-PDT) selectively targets infected/abnormal epithelium and generates reactive oxygen species, offering advantages such as minimal damage to cervical structures and good overall safety. Previous studies have suggested that it can improve HR-HPV clearance rates and improve the local inflammatory environment [6-8]. However, in clinical practice, persistent viral load or follow-up recurrence cases still occur after PDT, suggesting that local clearance alone may not be sufficient to fully correct the imbalance between inflammation, immunity, and microecology [7]. Kangfuxin solution has mucosal repair, anti-inflammatory, and immunomodulatory effects, and can improve symptoms related to chronic cervicitis and may increase the HPV seroconversion rate [9-13]. However, there is limited evidence regarding 5-ALA-PDT combined with oral Kangfuxin solution in HPV-positive cervical erosion patients, and a comprehensive evaluation of virological outcomes, microecology, inflammatory markers, and quality of life is lacking.

Based on the aforementioned clinical challenges and evidence gaps, the innovation and clinical significance of this study lies in proposing and evaluating a synergistic strategy of “5-ALA-PDT local clearance combined with Kangfuxin solution systemic repair/immune modulation” from a real-world perspective. This approach aims to assess comprehensive benefits through multidimensional outcomes (HR-HPV seroconversion/recurrence microecology, inflammatory factors, and SF-36 quality of life) that better meet clinical decision-making needs. This provides a treatment approach for HPV-positive cervical erosion patients that may improve seroconversion and reduce the risk of recurrence results without significantly increasing adverse reactions. Therefore, this retrospective study compared the efficacy and safety of 5-ALA-PDT combined with oral Kangfuxin solutions versus 5-ALA-PDT alone, and used propensity score matching (PSM) to reduce confounding bias in treatment selection, aiming to provide evidence-based support

for the comprehensive management of HPV-positive cervical erosion.

Materials and methods

Patient selection

This was a single-center retrospective study. Electronic medical records from the Department of Traditional Chinese Gynecology at the Fourth Hospital of Shijiazhuang City were retrieved, including outpatient medical records, colposcopy records, cervical cytology/pathology reports, and laboratory test results. We collected data from patients with cervical erosion who visited the hospital between January 2022 and December 2024. Systematic screening was performed using keywords and criteria such as “human papillomavirus (HPV), positive by Hybrid Capture 2 assay (HC2)”, “cervical erosion/cervical columnar epithelial ectopia/chronic cervicitis”, and “5-ALA photodynamic therapy records”. The initial screening included 314 cases, from which 32 cases were excluded according to the exclusion criteria. Among these, 11 cases had cervical intraepithelial neoplasia grade 2 or higher (CIN2+) or cervical malignancy; 8 cases had used other anti-HPV treatments or vaginal medications within the past 3 months; 7 cases had severe immune diseases or long-term immunosuppressive therapy; and 6 cases had severe liver or kidney dysfunction. The final pre-matching cohort consisted of 282 cases (129 in the observation group and 153 in the control group).

Treatment regimens in this study were not randomly assigned, but determined jointly by attending physicians and patients based on real-world clinical practice. Before treatment, physicians fully explained to patients the treatment principles, potential benefits, limitations, and possible adverse reactions of 5-ALA-PDT monotherapy and 5-ALA-PDT combined with oral Kangfuxin solution. Patients chose their treatment regimen based on their full understanding and clinical condition.

Given that the retrospective design, the choice of treatment regimen may lead to baseline differences. To reduce the influence of selection bias and confounding factors, this study further used PSM to construct a matching cohort of 226 cases (113 cases in the observation group and 113 cases in the control group) as the main analysis subjects. The specific research

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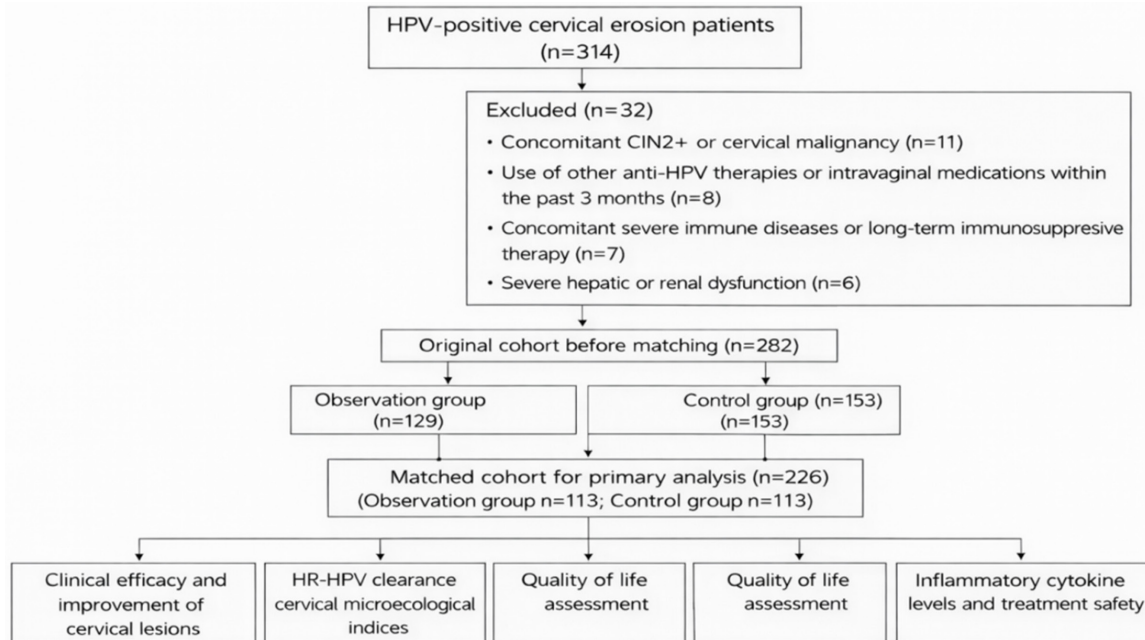


Figure 1. Research flowchart.

process is shown in **Figure 1**. This study was approved by the Ethics Committee of the Fourth Hospital of Shijiazhuang City (No.: 2020-0056). Inclusion criteria: (1) age 18-55 years; (2) colposcopy showing cervical erosion-like changes; (3) positive HR-HPV DNA detected by HC2 assay; (4) no high-grade squamous intraepithelial lesion (HSIL) or higher on ThinPrep cytologic test (TCT); (5) completed at least three sessions of PDT and follow-up [11]. Exclusion criteria: (1) pregnancy or lactation; (2) CIN2+ or cervical malignancy; (3) severe immune disease or long-term immunosuppressive therapy; (4) use of other anti-HPV treatments or vaginal medications within the past 3 months; (5) severe hepatic or renal dysfunction.

Treatment methods

Patients in the control group received 5-ALA-PDT treatment using 20% ALA gel (National Drug Approval No. H20070027; Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co., Ltd.). After emptying the bladder and thoroughly cleaning cervical secretions, the gel was evenly applied to the cervical surface and cervical canal and then sealed to protect from light for 4 h. Subsequently, photodynamic therapy (National Medical Device Registration Certificate 20163240995, Guilin Xingda Optoelectronic Medical Device Co., Ltd.) was used to

provide 630 nm laser irradiation at an energy density of 100 J/cm², once every 2 weeks for a total of 3 courses. Laser irradiation was administered under direct colposcopic visualization. The irradiation field was centered on regions of cervical erosion-like changes (columnar epithelial ectopy), encompassing the visible lesion surface and the complete transformation zone. For lesions of greater extent, treatment was delivered via multi-site, segmented irradiation with adequate overlap between adjacent fields, which guaranteed uninterrupted coverage of the entire visible erosion-like lesion area. The operator recorded the irradiated sites and coverage extent, with specific documentation of coverage for the periphery of the external cervical os and the endocervical os region, in the official procedure documentation, thereby optimizing the reproducibility of the technique. The observation group received the above 5-ALA-PDT regimen plus 10 mL of Kangfuxin solution (Sichuan Haoyisheng Panxi Pharmaceutical Co., Ltd.; National Drug Approval No. Z51021834) orally once daily for 3 consecutive months.

Data extraction and quality control

Two uniformly trained researchers independently extracted data from the electronic medical record system according to a pre-defined data extraction table. This included demo-

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graphic and baseline information (age, body mass index, disease duration, age at first delivery, number of deliveries, history of miscarriage, smoking history, oral contraceptive use, etc.), treatment information, laboratory and examination results, inflammatory factor levels, quality of life scores, and adverse reaction records. If the extraction results from the two researchers were inconsistent, a third researcher reviewed the original medical records to make a determination. For cases included in the primary analysis cohort, ID deduplication and missing value checks were performed, and the primary outcome indicators and covariates were recorded completely. To reduce the influence of inter-operator variability on therapeutic efficacy assessment, our institute implemented a standardized operating procedure for ALA-PDT, which specified the topical application range (cervical surface and cervical os), duration of light-protected occlusion, irradiation energy density, and rules for irradiation coverage including zonal overlap and complete coverage of all visible erosion-like lesions and the transformation zone. Procedures were carried out exclusively by colposcopists who had undergone standardized training, and all critical parameters and irradiation coverage were prospectively documented in medical and treatment records using standardized forms.

Outcome measures

Primary outcome measures: (1) Efficacy assessment: "Cure" was defined as complete disappearance of clinical symptoms, cervical erosion no longer visible, smooth and pinkish-white cervical surface, no congestion or scarring of the mucosa, and good coverage of new squamous epithelium; "Improvement" was defined as a reduction in the area of cervical erosion and a significant improvement in clinical symptoms; "Ineffective" was defined as failure to meet any of the above criteria. The formula for calculating the total effective rate was: Total effective rate = (number of cured cases + number of improved cases)/total number of cases × 100% [14]. (2) Cervical microecology: Vaginal pH, hydrogen peroxide (H₂O₂), and lactobacillus levels were measured in both groups before treatment and 3 months after treatment. Vaginal secretions were collected 3-5 days after menstruation and sent for testing within 2 h. (3) Vaginal cleanliness: Vaginal secretions were collected from both groups

before treatment and 3 months after treatment, and the vaginal cleanliness was recorded: Grade I-II was recorded as negative, and Grade III-IV as positive [15]. (4) Cervical erosion degree: The degree of cervical erosion was recorded from both groups before treatment and 3 months after treatment. The degree of erosion was graded by a colposcope-trained physician based on the proportion of the erosion-like change area to the visible area of the external cervical os: >2/3 was severe, 1/3-2/3 was moderate, and <1/3 was mild; standardized images were retained for verification when necessary, and a second colposcopist re-graded the erosion degree to reduce inter-assessor variability. (5) Negative conversion rate and recurrence rate of HR-HPV: HR-HPV DNA was detected by the HC2 assay before treatment, 3 months, and 6 months after treatment. After the cervix was exposed using a speculum, a qualified, regularly trained personnel used a disposable cervical brush (CooperSurgical Inc. (USA), CFDA Import Permit No. 20102661827) to collect samples by rotating the brush clockwise 3-5 times at the cervical os. The brush head was immediately immersed in HC2-specific preservation solution and labeled. The samples were then analyzed according to the established procedure. Results were expressed as a relative luminescence unit/threshold ratio. A ratio <1.0 was considered negative; a ratio ≥1.0 was considered positive. The 3-month negative conversion rate = number of negative cases at 3 months/total number of cases; the 6-month sustained negative conversion rate = number of negative cases at 6 months/total number of cases; the recurrence rate = number of cases that were negative at 3 months but became positive at 6 months/number of negative cases at 3 months.

Secondary outcome measures: (1) Quality of life: The SF-36 questionnaire was used to evaluate and compare quality of life in the two groups of patients before and 3 months after treatment. The Cronbach's α coefficient was 0.75, the structural coefficient was 0.825, and the full score was 100. The higher the score, the higher the quality of life in the relevant dimension [16]. (2) Inflammatory markers: Before treatment and 3 months after treatment, blood samples (5 mL) were collected from the peripheral veins of both groups in the morning under fasting conditions. After standing at room temperature for approximately 30

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min, the serum was separated by centrifugation at 3,000 r/min (centrifuge: Eppendorf, model 5427 R) for 10 min and stored in a -80°C refrigerator (Haier, model DW-86L626) for testing. The serum levels of interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and C-reactive protein (CRP) were detected by enzyme-linked immunosorbent assay (ELISA). The IL-6 kit was purchased from Xinbosheng Biotechnology Co., Ltd. (Cat. No. EMC004.96); the TNF- α kit was purchased from Wuhan Elabscience Biotechnology Co., Ltd. (Cat. No. E-EL-H0109c); and the CRP kit was provided by Wuhan Huamei Bioengineering Co., Ltd. (Cat. No. CSB-E08617h). (3) Adverse reactions: The occurrence of adverse reactions such as local burning/pain, increased secretions, spotting bleeding, abdominal distension, and nausea during the 3-month treatment period was recorded.

Statistical analysis

Statistical analyses were performed using SPSS version 20.0 software. Continuous variables were expressed as mean \pm standard deviation ($\bar{x} \pm s$). Independent samples t-tests were used for comparisons between groups, and paired t-tests were used for comparisons before and after treatment. Categorical variables were presented as frequencies and percentages (n, %), and differences between groups were assessed using the χ^2 test. PSM was performed using logistic regression to estimate propensity scores, with treatment group as the dependent variable (coded 1 for Kangfuxin solution combined therapy, 0 for ALA-PDT monotherapy). Baseline covariates assessed prior to matching included: age, BMI, disease duration (years), age at first delivery, number of deliveries, miscarriage history, smoking history, oral contraceptive use, baseline vaginal cleanliness grade, baseline vaginal pH, baseline vaginal H₂O₂ level, baseline lactobacillary status, baseline severity of cervical erosion-like changes/ectropion (mild/moderate/severe), and baseline inflammatory factors (TNF- α , IL-6, CRP). A 1:1 nearest-neighbor matching scheme without replacement was applied to establish the matched cohort. As this study was based on retrospective electronic health record data, the variable for HPV infection duration, defined as the interval between first HR-HPV detection and treatment, was unavailable and therefore excluded from the PSM model. To mitigate potential residual

confounding after matching, particularly the trend in baseline differences in cervical erosion-like changes/ectropion severity, a doubly robust sensitivity analysis with regression adjustment was further performed in the PSM-matched cohort. For the primary endpoint, key covariates including treatment group, age, BMI, disease duration, and baseline cervical erosion/ectropion severity were incorporated as adjustment factors in the regression model. $P < 0.05$ was considered statistically significant.

Results

Comparison of general baseline data

There were no statistically significant differences between the two groups in general characteristics such as age, body mass index, age at first delivery, number of deliveries, history of miscarriage, smoking, and use of oral contraceptives (all $P > 0.05$), therefore comparisons between the two groups were possible. See **Table 1**.

Comparison of clinical efficacy

The efficacy rate in the observation group was 96.46%, while it was 80.53% in the control group ($P < 0.001$). See **Table 2** and **Figures 2-4**.

Comparison of cervical microecology

After treatment, the vaginal pH value of both groups decreased compared to before treatment, and the H₂O₂ positivity rate and abnormal lactobacillus rate also decreased compared to baseline. Furthermore, all of these indicators in the observation group were lower than those in the control group (all $P < 0.001$), as shown in **Table 3**.

Comparison of vaginal cleanliness

After treatment, the vaginal cleanliness of both groups significantly improved compared to before treatment, with the observation group showing a greater degree of improvement than the control group ($P < 0.001$), as shown in **Table 4**.

Severity of cervical erosion

Before treatment, there was no statistically significant difference in the degree of cervical erosion between the two groups. After 3 months of

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Table 1. General baseline data (n, $\bar{x} \pm s$)

Indicator	Observation Group (n=113)	Control group (n=113)	χ^2/t	P
Age (years)	39.5±8.3	40.5±7.8	0.968	0.334
Body mass Index (kg/m ²)	22.68±3.06	22.94±2.66	0.692	0.490
Course of the disease (years)	1.92±0.84	2.02±0.82	0.878	0.381
Age at first childbirth (years)	25.66±3.44	24.87±2.78	1.915	0.057
Number of deliveries (times)	1.67±0.92	1.85±0.90	1.463	0.145
History of miscarriage			0.075	0.784
No	71	69		
Yes	42	44		
Smoking situation			0.064	0.801
No	104	105		
Yes	9	8		
The use of oral contraceptives			0.042	0.838
No	99	100		
Yes	14	13		

Table 2. Comparison of clinical efficacy between the two groups (n, %)

Group	Cure	Improvement	Ineffective	Total Effective
Control group (n=113)	43 (38.05)	48 (42.48)	22 (19.47)	91 (80.53)
Observation Group (n=113)	56 (49.56)	53 (46.90)	4 (3.54)	109 (96.46)
χ^2				14.082
P				<0.001

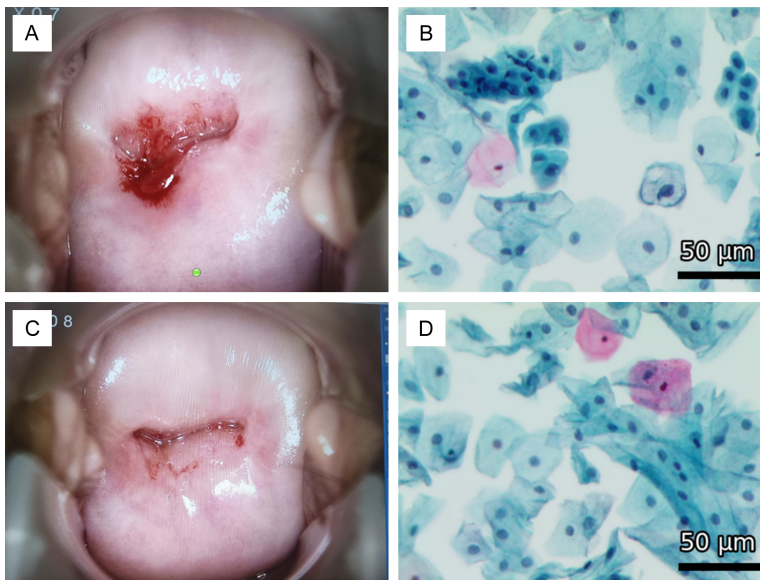


Figure 2. Clinical outcomes in patients with mild cervical erosion. A: Colposcopic findings before treatment; B: TCT results before treatment; C: Colposcopic findings after treatment; D: TCT results after treatment. TCT, Thin-Prep cytologic test.

groups, and the improvement in erosion severity was greater in the observation group ($P < 0.001$), as shown in **Table 5**. After matching, the proportion of severe erosion/erosion at baseline in the observation group was slightly higher than that in the control group (23.89% vs 16.81%), suggesting that residual imbalance persisted. Considering that the degree of baseline erosion/erosion may affect HPV outcomes and repair results, this study further conducted a sensitivity analysis of regression correction (double robustness) in the PSM-matched cohort to verify the consistency of the results.

Comparison of HR-HPV negative conversion rates

treatment, there was a significant difference in the degree of cervical erosion between the two

After 3 months of treatment, the HR-HPV negative conversion rate in the observation group

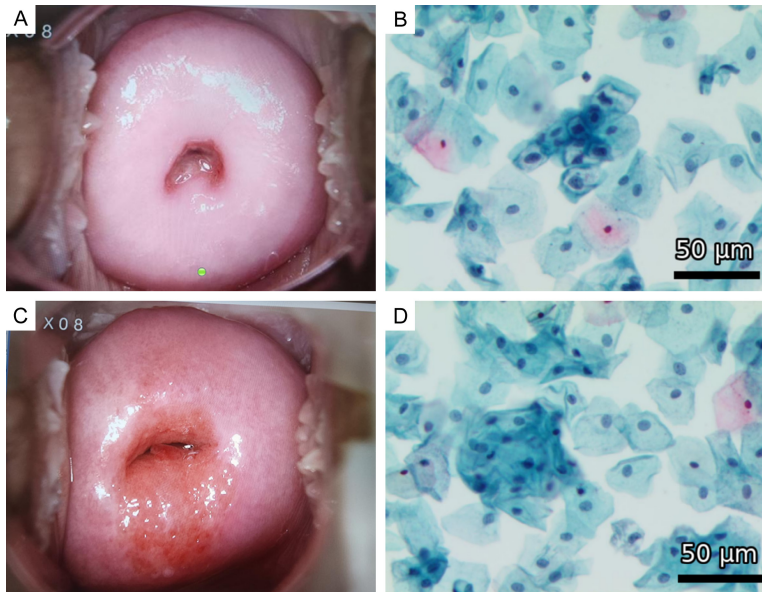


Figure 3. Clinical outcomes in patients with moderate cervical erosion. A: Colposcopic findings before treatment; B: TCT results before treatment; C: Colposcopic findings after treatment; D: TCT results after treatment. TCT, ThinPrep cytologic test.

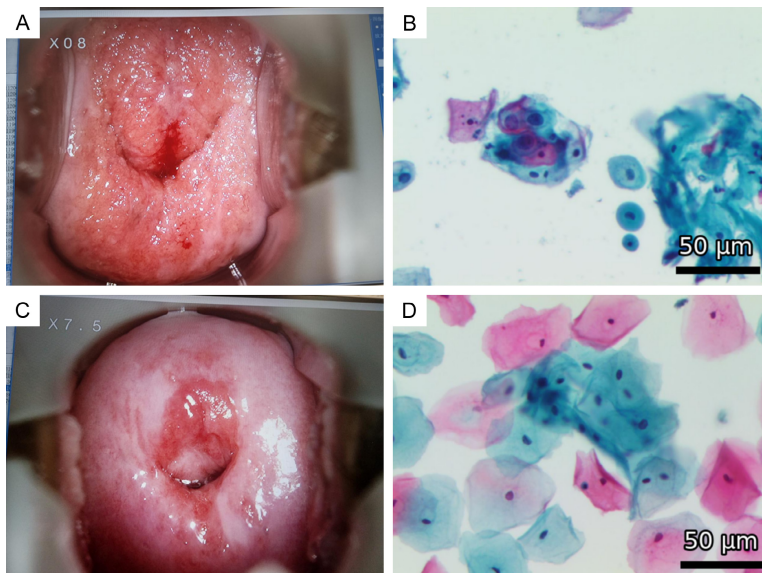


Figure 4. Clinical outcomes in patients with severe cervical erosion. A: Colposcopic findings before treatment; B: TCT results before treatment; C: Colposcopic findings after treatment; D: TCT results after treatment. TCT, ThinPrep cytologic test.

was 80.5%, significantly higher than that in the control group ($\chi^2=8.364$, $P=0.004$). During the 6-month follow-up, 7 cases of recurrence of cervical erosion occurred in the observation group, while 19 cases occurred in the control group. The difference in recurrence rates

between the two groups was statistically significant ($\chi^2=10.582$, $P=0.001$), as shown in **Table 6**. A multi-factor Logistic regression model was further constructed in the PSM-matched cohort (to avoid overfitting due to the small number of recurrence events, the model included treatment groups and adjusted for age, BMI, disease duration, and baseline erosion/erosion degree). The results showed that: combined oral Kangfuxin solution was still independently associated with 3-month HR-HPV negativity (adjusted OR=2.27, 95% CI 1.24-4.16, $P=0.008$); among those who turned negative at 3 months, the combined regimen was independently associated with a reduced risk of 6-month recurrence (adjusted OR=0.22, 95% CI 0.09-0.55, $P=0.001$), suggesting that the conclusion is robust.

Comparison of serum IL-6, TNF- α , and CRP levels

After treatment, the levels of IL-6, TNF- α , and CRP decreased in both groups compared to before treatment, and the degree of reduction in these inflammatory indicators was significantly better in the observation group than in the control group (all $P<0.001$). See **Table 7**.

Comparison of quality of life

Before treatment, there were no statistically significant differences in the scores of the two groups on the SF-36 scale across dimensions such as physical function, overall health, social function, emotional role, and mental health (all $P>0.05$). After treatment, the scores of all dimensions in both groups were significantly improved compared to before the intervention, and the scores of the observa-

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Table 3. Comparison of cervical microecology between the two groups

Group	pH value		Positive rate of H ₂ O ₂ n (%)		Abnormal rate of Lactobacillus n (%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=113)	5.62±0.16	4.39±0.30*	108 (95.58)	48 (42.48)*	105 (92.92)	43 (38.05)*
Observation Group (n=113)	5.59±0.12	4.25±0.21*	105 (92.92)	24 (21.24)*	110 (97.35)	8 (7.08)*
χ ² /t	1.616	4.081	0.735	11.740	2.389	31.020
P	0.108	<0.001	0.391	0.001	0.122	<0.001

Note: Compared with the same group before treatment, *P<0.05. H₂O₂: hydrogen peroxide.

Table 4. Comparison of vaginal cleanliness before and after graded treatment in the two groups [n (%)]

Index	Control group (n=113)	Observation Group (n=113)	χ ²	P	
Before treatment	Grade I	0 (0.00)	0 (0.00)	2.187	0.335
	Grade II	29 (25.66)	35 (30.97)		
	Grade III	67 (59.29)	56 (49.56)		
	Grade IV	17 (15.04)	22 (19.47)		
	Normal rate Grade I-II	29 (25.66)	35 (30.97)		
After treatment	Grade I	26 (23.01)	40 (35.40)	22.224	<0.001
	Grade II	61 (53.98)	70 (61.95)		
	Grade III	19 (16.81)	3 (2.65)		
	Grade IV	7 (6.19)	0 (0.00)		
	Normal rate Grade I-II	87 (76.99)*	110 (97.35)*		

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

Table 5. Comparison of the degree of cervical erosion between the two groups (n, %)

Group	Before treatment			After treatment		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Control group (n=113)	13 (11.50)	81 (71.68)	19 (16.81)	62 (54.87)*	45 (39.82)*	6 (5.31)*
Observation Group (n=113)	11 (9.73)	75 (66.37)	27 (23.89)	89 (78.76)*	24 (21.24)*	0 (0.00)*
χ ²	1.789			17.219		
P	0.409			<0.001		

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

Table 6. Comparison of HR-HPV negative conversion and recurrence cases in the two groups

Group	3 months negative conversion n (%)	6 months recurrence n (%)
Control group (n=113)	72 (63.7)	19 (26.4)
Observation Group (n=113)	91 (80.5)	7 (7.7)
χ ²	8.364	10.582
P	0.004	0.001

Note: HR-HPV, high-risk human papillomavirus.

Multivariate logistic regression analysis of intervention effect

In the primary analysis cohort after PSM (n=226), we performed a multivariate logistic regression analysis with overall response (recovery/improvement) as the dependent variable, incorporating treatment groups and baseline covariates. The results showed that combined oral Kangfuxin solution was independently associated with a higher overall response rate (OR=7.421, 95% CI 2.348-23.460, P<0.001). No statistically significant associations were

tion group were significantly higher than those of the control group in all dimensions (all P<0.001) (Table 8).

associated with a higher overall response rate (OR=7.421, 95% CI 2.348-23.460, P<0.001). No statistically significant associations were

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Table 7. Comparison of serum inflammatory indicators between the two groups ($\bar{x} \pm s$)

Group	TNF- α (ng/L)		CRP (mg/L)		IL-6 (pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=113)	103.23 \pm 35.52	50.90 \pm 4.04*	19.14 \pm 2.66	5.28 \pm 1.11*	15.38 \pm 3.84	8.40 \pm 2.70*
Observation Group (n=113)	110.23 \pm 53.16	47.43 \pm 3.38*	19.10 \pm 2.18	4.12 \pm 1.08*	16.11 \pm 3.69	6.20 \pm 2.34*
t	1.164	-6.992	0.118	-7.936	1.450	-6.541
P	0.246	<0.001	0.907	<0.001	0.148	<0.001

Note: Compared with the same group before treatment, *P<0.05. IL-6, Interleukin-6; TNF- α , tumor necrosis factor- α ; CRP, C-reactive protein.

Table 8. Comparison of SF-36 quality of life scores between the two groups (points, $\bar{x} \pm s$)

Group	Control group (n=113)	Observation Group (n=113)	t	P
Physical Functioning				
Before treatment	61.51 \pm 7.93	62.65 \pm 7.16	-1.127	0.261
After treatment	66.53 \pm 8.80*	78.13 \pm 10.84*	8.836	<0.001
General Health				
Before treatment	81.08 \pm 9.41	80.35 \pm 11.81	-0.511	0.61
After treatment	84.62 \pm 9.75*	92.05 \pm 5.79*	6.967	<0.001
Social Functioning				
Before treatment	60.44 \pm 10.77	60.05 \pm 9.62	-0.286	0.775
After treatment	66.21 \pm 11.28*	73.17 \pm 10.89*	4.715	<0.001
Role Emotion				
Before treatment	50.73 \pm 8.11	49.50 \pm 8.64	-1.112	0.267
After treatment	55.38 \pm 7.88*	65.31 \pm 9.58*	8.506	<0.001
Mental Health				
Before treatment	49.50 \pm 7.06	49.61 \pm 7.45	0.11	0.912
After treatment	57.50 \pm 7.52*	70.21 \pm 11.99*	9.55	<0.001
Physical Functioning				
Before treatment	61.51 \pm 7.93	62.65 \pm 7.16	-1.127	0.261
After treatment	66.53 \pm 8.80*	78.13 \pm 10.84*	8.836	<0.001

Note: Compared with the same group before treatment, *P<0.05. SF-36, 36-Item Short Form Health Surve.

observed between the remaining covariates and overall response rate (P>0.05). This model was adjusted by incorporating covariates such as the degree of baseline erosion/erosion (mild/moderate/severe) (Table 9).

Comparison of adverse reaction rates

During the treatment, there was no statistically significant difference in the total incidence of adverse reactions such as vaginal burning and pain, increased vaginal discharge, mild vaginal bleeding, and nausea between the two groups (all P>0.05), as shown in Table 10.

Discussion

This study included HPV-positive cervical erosion patients and compared the efficacy of combined oral Kangfuxin solution and PDT alone, based on the 5-ALA-PDT therapy. Results

showed that the observation group had a higher HR-HPV negative conversion rate at 3 months and a lower positive recurrence rate at 6 months, both significantly better than the control group. Simultaneously, the observation group showed greater improvement in cervical erosion repair, vaginal microecology, inflammatory factor levels, and SF-36 quality of life scores across all dimensions. The incidence of adverse reactions was similar in both groups, suggesting that the comprehensive treatment strategy of local 5-ALA-PDT combined with Kangfuxin liquid has a synergistic advantage in improving virological outcomes and promoting cervical mucosal repair. However, it should be noted that the primary analysis of this study was based on a 1:1 matched PSM cohort, with 113 cases in both the observation group and the control group; accordingly, the two groups had identical sample sizes after matching. By contrast, the original cohort comprised 129

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Table 9. Results of multivariate logistic regression analysis

Variable	OR (95% CI)	P
Treatment Group (Observation Group vs Control Group)	7.421 (2.348-23.460)	<0.001
Age (years)	1.014 (0.957-1.075)	0.632
Body Mass Index (kg/m ²)	0.874 (0.737-1.036)	0.121
Disease Duration (years)	1.216 (0.685-2.158)	0.505
Age at First Childbirth (years)	1.015 (0.873-1.181)	0.846
Number of Deliveries	1.316 (0.804-2.155)	0.275
Abortion History (Yes vs No)	0.750 (0.309-1.822)	0.526
Smoking (Yes vs No)	1.153 (0.218-6.102)	0.867
Oral Contraceptive Use (Yes vs No)	0.665 (0.189-2.342)	0.525
Baseline Erosion Degree (Moderate vs Mild)	0.669 (0.144-3.103)	0.608
Baseline Erosion Degree (Severe vs Mild)	1.170 (0.180-7.616)	0.870

Table 10. Comparison of adverse reactions between the two groups (n, %)

Group	Local burning/ pain	Increased vaginal discharge	Mild vaginal bleeding	Nausea/abdominal discomfort	Total
Control group (n=113)	7 (6.19)	4 (3.54)	2 (1.77)	1 (0.88)	14 (12.39)
Observation Group (n=113)	6 (5.31)	4 (3.54)	1 (0.88)	2 (1.77)	13 (11.50)
χ^2					0.405
P					0.525

cases in the observation group and 153 cases in the control group before matching. Although PSM reduces baseline differences, treatment selection bias and confounding bias to a certain extent, thereby enhancing the comparability and interpretability of the results, its findings should still be interpreted cautiously in light of the inherent limitations of retrospective studies.

In this study, there were no statistically significant differences between the observation and control groups in terms of general baseline data such as age, body mass index, menstrual and reproductive history, smoking, and use of oral contraceptives. This indicates that the two groups were comparable in terms of major demographic and clinical characteristics, which can reduce the interference of confounding factors on the outcome indicators to a certain extent. Furthermore, the overall response rate in the observation group was significantly higher than that in the control group, and the proportion of cervical erosion transforming from moderate to severe to mild or cured was higher, further confirming that combining systemic medication with local photodynamic therapy helps to achieve faster and more complete cervical epithelial repair.

Multiple clinical studies have confirmed the efficacy of 5-ALA-PDT in the treatment of HPV-related cervical lesions. This therapy can achieve a high lesion regression rate and HPV clearance rate while preserving the cervical anatomy and fertility. Previous literature has reported that the HPV negative conversion rate was mostly in the range of 60% to 80% at 3-6 months of follow-up [17-20]. In this study, the HR-HPV negative conversion rate in the control group at 3 months post-treatment was 63.7%, which is basically consistent with the above-mentioned range, suggesting that the 5-ALA concentration, irradiation wavelength, and energy density, are representative. On this basis, this study further combined oral Kangfuxin solution treatment, and the HR-HPV negative conversion rate in the observation group at 3 months post-treatment significantly increased to 80.5%. When the evaluation criterion was negative conversion at 3 months post-treatment with continuous follow-up to 6 months, the sustained negative rate in the observation group was significantly higher than that in the control group, and the recurrence rate was also significantly lower. The above findings suggest that combining Kangfuxin solution with the standard 5-ALA-PDT regimen may further optimize virological treatment out-

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comes and reduce the risk of early seroconversion without increasing local cervical trauma and invasiveness. However, this study adopted the HC2 assay to detect the overall load of HR-HPV, but lacked genotyping analysis and genotype-specific outcome analysis. The differences in clearance rates among different HPV genotypes may affect HPV clearance and recurrence performance, and further validation combined with genotyping is still required in subsequent studies.

Studies have found that PDT alone can significantly reduce pro-inflammatory factors such as TNF- α and IL-6, and combining it with Kangfuxin solution may further enhance anti-inflammatory effects through multi-target synergy [21, 22]. Our results show that IL-6, TNF- α , and CRP levels significantly decreased in both groups after treatment, with a more significant decrease in the observation group. Based on the premise that PDT selectively clears HPV infection and inflammatory cells through reactive oxygen species and reduces persistent antigen and inflammatory stimulation, Kangfuxin solution promotes cervical mucosal blood supply and epithelial regeneration, accelerating wound healing. Additionally, it may further downregulate pro-inflammatory mediator levels by inhibiting inflammatory signaling pathways such as NF- κ B and improving Th1/Th2 and innate immune balance, thus forming a synergistic effect of “local burden reduction + systemic regulation”, making the overall anti-inflammatory and immunomodulatory effects more significant. However, this study detected peripheral blood system inflammatory markers, which can reflect changes in overall inflammatory load, but the “in situ evidence” of cervical local immunity and mucosal inflammation is still relatively insufficient. Further supplementation with local cytokines, immune cell subsets, or mucosal immunity-related indicators will help elucidate the mechanistic basis of the combined regimen’s benefits.

Studies have found that persistent HPV infection is closely related to vaginal and cervical microecological imbalance. A decrease in dominant lactobacilli, an increase in vaginal pH, and excessive growth of opportunistic pathogens can all promote viral persistence and damage the epithelial barrier, thereby increasing the risk of CIN and cervical cancer [23, 24]. The results of this study showed that vaginal pH lev-

els in both groups decreased significantly after treatment compared to baseline, and the H₂O₂ positivity rate and abnormal lactobacillus rate significantly decreased, suggesting that photodynamic therapy can improve the local cervical microecology by clearing infected epithelium, inhibiting pathogenic microorganisms, and promoting epithelial barrier reconstruction. Further comparison revealed that the observation group showed greater improvement in the above indicators than the control group, with a significantly increased proportion of vaginal cleanliness grades I-II, a marked migration of cervical erosion from moderate to severe to mild, and a significantly increased cure rate, reflecting the superior advantages of the combined regimen in restoring local microbial balance and mucosal barrier function. Furthermore, the meaning of “positive/negative” for microecological related test items may differ across different platforms/reagents; the interpretation of results should strictly adhere to the testing methods and interpretation criteria used in this study. Nevertheless, the consistent trends in pH decrease, cleanliness improvement, and the decrease in the abnormal lactobacillus rate still support the combined regimen’s role in promoting microecological reconstruction.

This study used the SF-36 scale to assess patients’ quality of life across multiple dimensions, including physical, psychological, and social functioning. The SF-36 scale is one of the most widely used health-related quality of life assessment tools internationally, and its high reliability and validity have been demonstrated in various population groups. The results of this study showed that the scores of the two groups were roughly equivalent in each dimension before treatment. After 3 months of treatment, the quality of life scores of both groups improved compared with the baseline, but the observation group showed significantly better improvement in the dimensions of physical function, overall health, social function, emotional role and mental health than the control group. Cervical erosion and HPV positivity can not only lead to physical symptoms such as abnormal vaginal discharge and vaginal discomfort, but are also often accompanied by anxiety and shame about the progression of cervical cancer, which has an adverse effect on women’s mental health and participation in social roles. Previous studies have pointed out

that HPV positivity can significantly increase patients' anxiety and worry, especially when there is a lack of sufficient understanding of the characteristics and prognosis of the virus [25]. The findings of this study suggest that while improving local lesions and increasing the virological conversion rate, PDT combined with Kangfuxin solution can also promote the dual physiological and psychological benefits of patients by alleviating symptoms, optimizing vaginal microecology and inflammatory status, thereby improving the overall quality of life. Regarding safety, no serious adverse events occurred in either group during the treatment process in this study. The main adverse reactions were mild local burning/pain, temporary increase in secretions, and mild abdominal distension and nausea. The adverse reactions were all mild, some of which resolved spontaneously, and the rest disappeared after simple symptomatic treatment. The difference in the total incidence of adverse reactions between the two groups was not statistically significant. Previous systematic reviews and prospective studies have also pointed out that the adverse reactions of 5-ALA-PDT are mainly transient local discomfort, and serious complications are rare [26]. Kangfuxin solution has also demonstrated good safety in oral or local application in various diseases such as digestive tract, oral cavity and gynecology [27]. The results of this study are basically consistent with the aforementioned literature, which further supports the tolerability and safety of this combined regimen in patients with HPV-positive cervical erosion.

This study still has certain limitations. First, the single-center retrospective design inherently carried selection and information bias, even though baseline characteristics were largely balanced between the two groups. Conclusions drawn herein therefore require validation in large-scale, multicenter prospective randomized controlled trials. Second, the 6-month follow-up was insufficient to comprehensively assess long-term sustained HR-HPV clearance, as well as the potential progression or recurrence of CIN. Third, only a limited panel of inflammatory markers (IL-6, TNF- α , and CRP) was measured, with no in-depth evaluation of immune cell subsets, mucosal immune mediators, or HPV genotyping profiles. Future mechanistic studies are encouraged to integrate flow

cytometry and multi-omics approaches to delineate underlying pathways from immunological and microecological perspectives. Fourth, HR-HPV burden was evaluated solely by HC2 testing without concurrent genotyping, restricting the analysis of genotype-specific differences and outcome heterogeneity. Efficacy assessments and corresponding endpoints were also susceptible to variations in medical record completeness and inter-assessor variability; while consistency checks and quality control were applied during data extraction, these findings warrant corroboration in higher-quality investigations. Fifth, as a real-world retrospective study, treatment regimens were determined jointly by clinicians and patients, so unmeasured confounders including patient compliance, health behaviors, and follow-up adherence may have influenced clinical outcomes. Although propensity score matching strengthened the robustness of the results, prospective research is still necessary to confirm causal associations and define the applicable patient population. Finally, while a unified standardized operating procedure was implemented and irradiation coverage rules documented consistently, the retrospective nature of the data prevented independent, repeated quantitative documentation of irradiation fields and segmented zones. Inter-operator reliability (e.g., intraclass correlation coefficient) was therefore unable to be assessed, which restricts rigorous validation of treatment parameter reproducibility. Standardized irradiation templates and formal consistency testing should be integrated into future prospective protocols.

In conclusion, adding oral Kangfuxin solution to standard 5-ALA-PDT treatment can further improve the HR-HPV negative conversion rate in HPV-positive cervical erosion patients without increasing significant adverse reactions; it promotes cervical erosion repair and vaginal microecological reconstruction, reduces systemic inflammation levels, and significantly improves patients' quality of life.

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Disclosure of conflict of interest

None.

Address correspondence to: Hongna Xiao and Yu Gao, Department of Traditional Chinese Medicine, Fourth Hospital, Shijiazhuang 050000, Hebei, China. Tel: +86-13483665200; E-mail: 13483665200@163.com (HNX); Tel: +86-13931-982083; E-mail: 686825@qq.com (YG)

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