

# Research and Nursing Experience of Recombinant Human Epidermal Growth Factor Gel Promoting Oral Mucosal Erosion Lesion Healing

Bo Yu  
Bing Xu  
Chonggui Qiu  
Yang Liu

Erosion is a primary clinical manifestation of oral mucosal lesions. Contact between food and the mucosal surface during chewing can easily cause oral mucosal infection and adversely affect the daily lives of patients. Conventional clinical treatment cannot overcome the problems of oral mucosal erosion. This study aimed to analyze the application effect of recombinant human epidermal growth factor (rhEGF) gel on oral mucosal erosion lesions. The subjects of this study were 120 patients with oral mucosal erosion lesions, who were divided, according to random number table method, into a contrast group and rhEGF group with 60 cases in each. The patients in the contrast group were treated with ethacridine lactate, and the rhEGF group patients were treated with rhEGF gel. Patients in both groups received corresponding nursing measures. Compared with the contrast group, the rhEGF group had a lower visual analog scale score, Reticulation/keratosis, erythema, and ulceration score, and inflammatory cytokine levels, as well as a higher total effective rate and faster patient recovery, indicating that the rhEGF gel had significant efficacy and is worthy of promotion.

**Keywords:** Recombinant Human Epidermal Growth Factor, Gel, Oral Mucosal Lesions, Healing, Nursing

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Oral mucosal erosion is a category of oral mucosal diseases that affects the superficial layer of the epithelium but does not damage the entire epithelium<sup>1</sup>. Affected patients often experience different degrees of pain and reduced oral function, including difficulty eating. These symptoms cause substantial inconvenience in daily life. The occurrence of oral mucosal erosion is related to many factors, among which living environment, mental status, immune function, and genetic factors are the most common. According to relevant data, if oral mucosal erosion is not cured timeously, it can lead to cancer<sup>2</sup>. This

causes a substantial psychological burden to patients and affects treatment. Currently, ethacridine lactate monohydrate is used in the clinical treatment of oral mucosal erosion lesions, and it has a positive effect on the erosion of oral mucosa, but shortcomings still exist in pain relief and the speed of wound healing<sup>3</sup>. Because the primary lesions are easily hidden in oral mucosal erosion, treatment faces substantial difficulties. Therefore, there is an urgent need for therapeutic drugs that can promote the healing of oral erosion mucosa and effectively relieve pain. Recombinant human epidermal growth factor (rhEGF) is a

Bo Yu<sup>#</sup>Intensive Care Unit, The Second Hospital Of DaLian Medical University, Dalian116022, Liaoning Province, China, Bing Xu<sup>\*</sup>Delivery Room, The Second Hospital Of DaLian Medical University, Dalian116022, Liaoning Province, China, Chonggui Qiu<sup>#</sup>Intensive Care Unit, The Second Hospital Of DaLian Medical University, Dalian116022, Liaoning Province, China, YangLiu Intensive Care Unit, The Second Hospital Of DaLian Medical University, Dalian116022, Liaoning Province, China, <sup>#</sup>These authors contributed equally to this work as co-first author, <sup>\*</sup>Corresponding author: Delivery Room, The Second Hospital Of DaLian Medical University, Dalian116022, Liaoning Province, China

polypeptide material formed by the dehydration and condensation of 53 amino acids with a relative molecular weight of about 6,000 Daltons. It is the primary component of rhEGF gel, which promotes the repair and regeneration of mesoderm and ectoderm cells, and it can improve local blood circulation and facilitate rapid wound healing<sup>4</sup>. Clinically, it is primarily used in the healing of several wounds, including fresh wounds, chronic wounds, burn wounds, and chronic ulcer wounds. It also has certain curative effects on senile pruritus, dermatitis and sebum deficiency eczema<sup>5</sup>. Among these, mucosal ulcers are formed by the depression caused by the damage and shedding of both the mucosa and surface, and the disease is more severe than mucosal erosion<sup>6</sup>. Currently, there are few reports on the effect of rhEGF gel in treating oral mucosal erosion lesions. Therefore, this study aimed to explore the influence of rhEGF gel on wound healing in patients with oral mucosal erosion lesions to provide clinical reference for the treatment of patients.

## MATERIALS AND METHODS

### General Information of Patients

This study was approved by the Medical Ethics Committee. Patients admitted to the 2nd Affiliated Hospital of Harbin Medical University from May 2017 to May 2020 with oral mucosal erosion lesions were selected as the study objects. There were five criteria for the inclusion of patients: (1) they were clinically diagnosed with oral mucosal erosion lesions<sup>7</sup>, (2) they have received no mouth treatment drugs in the past month; (3) the duration of onset was <3 days; (4) they did not have any mental illness or cognitive impairment, and (5) they signed the informed consent. Additionally, there were four conditions of excluding patients: (1) they had contraindications to the drug used in this study, (2) they had complicated tuberculosis; (3) they had severe organic lesions of the heart, liver, kidney, and other important organs, and (4) they were pregnant or lactating women. A total of 120 patients were included and divided between the contrast group (n = 60) and rhEGF group (n = 60) using a random number table method. There was no significant difference in gender, age, and onset time between the two groups ( $P > 0.05$ ), and the groups were comparable in age and sex (Table 1).

Table 1.  
Sex, age, and disease time characteristics of the two treatment groups

Group	Gender (case, %)		Age (year, $\bar{x} \pm s$ )	Disease time (d, $\bar{x} \pm s$ )
	Male	Female		
Contrast group (n = 60)	27 (45.0)	33 (55.0)	37.55 $\pm$ 7.22	2.17 $\pm$ 0.21
rhEGF group (n = 60)	31 (51.67)	29 (48.33)	37.64 $\pm$ 7.15	2.23 $\pm$ 0.19
$\chi^2/t$	0.534		0.069	1.641
$P$	0.465		0.945	0.103

Note. rhEGF: Recombinant human epidermal growth factor.

### Research Method

A flow chart of the study is presented in Figure 1. The contrast group was treated with ethacridine lactate (manufacturer: Guangdong Nanguo Pharmaceutical Co., Ltd.; SDA (State Drugs Administration) License No.: GUOYAOZHUNZIH44024650; specifications: 0.1%). Three times each day, after routine cleaning of the oral mucosal erosion, gauze was dipped in ethacridine lactate and a wet compress was given to the patient for 30 min. The rhEGF group was treated with rhEGF gel (manufacturer: China

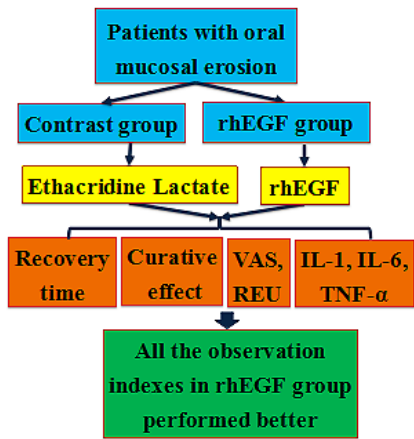
Guilin HuaNuowei Gene Pharmaceutical Co., Ltd.; SDA (State Drugs Administration) License No.: S20020111; specification: 10 g; Figure 2). Routine cleaning of the oral mucosal erosion was performed, followed by cleaning with normal saline. Then, according to the wound area, a recommended dose of 1 g/cm<sup>2</sup> rhEGF was rubbed in evenly, once a day. Both groups were treated continuously for 7 d.

Four nursing measures were applied. The first nursing measure was psychological nursing. Patients with oral mucosal erosion are often in different degrees of pain, which has a substantial impact on oral function, resulting in eating

difficulties. Additionally, there is a risk of cancer erosion. Therefore, the psychological burden of patients is aggravated, which is not conducive to improving health. As such, the nursing staff actively provided psychological counseling tailored to each patient's situation, and they encouraged family members to communicate with the patients to make them feel the care of their relatives and help them build up confidence in the successful treatment of the disease. Secondly, nursing during treatment was undertaken. Nursing staff told family members to supervise the patients to take their medicine on time and according to the required amount. Additionally, they educated family members about the matters requiring attention in the use of drugs and close cooperation with family members to provide the patients with more attention and care. The third nursing measure was life care. One of the causes of oral mucosal erosion is the living environment, and poor living and eating habits are not conducive to the repair of oral mucosal erosion. Therefore, the nursing staff

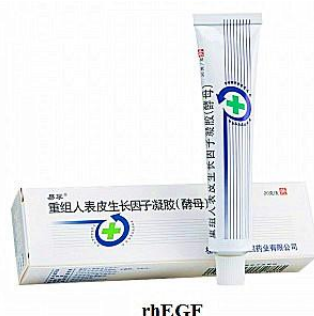
informed the family members of the dietary precautions, such as avoiding eating spicy, strong tasting, and stimulating food. The preferable diet is light with more vegetables and fruits and no alcohol. Additionally, patients should eat slowly, eat less coarse food, talk less to reduce oral mucosal friction, and clean their mouths out regularly, such as by gargling with light salt water after meals. The fourth nursing measure was daily oral care. Daily, in the morning and before bedtime, patients used nano-silver antibacterial mouthwash (manufacturers: Kunming Hande Nano Biotechnology Co., Ltd.; approval number: Yun Weixiao Certificate(2008) No.0026; specifications: 30 mL; Figure3) for oral care <sup>8,9</sup>. The nano-silver antibacterial mouthwash was sprayed into the lining of the mouth. It was also used for gargling or diluted to brush the teeth, being careful not to swallow the mouthwash. The nursing staff and the families of the patients provided close supervision of the treatment.

Figure 1.  
Research flow chart.



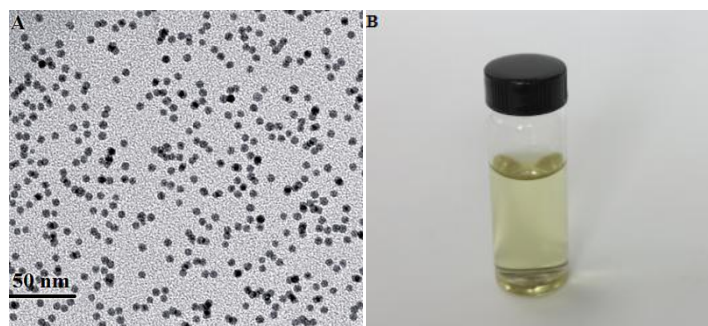
rhEGF: Recombinant human epidermal growth factor. VAS: Visual Analog Scale. IL-1: Interleukin-1. IL-6: Interleukin-6. TNF- $\alpha$  Tumor necrosis factor- $\alpha$  The subjects of this study were patients with oral mucosal erosion lesions. After grouping, they were given ethacridine lactate treatment and rhEGF gel treatment in the contrast and rhEGF gel groups, respectively. The recovery time, efficacy, VAS score, REU score, IL-1, IL-6, TNF- $\alpha$  and other indices were observed in the two groups.

**Figure 2.**  
**Recombinant human epidermal growth factor gel (rhEGF).**



rhEGF gel is a colorless, odorless, transparent gel. The specification is 10 g/dose. Store at 2°C–8°C.

**Figure 3.**  
**Nano-silver.**



A: Nano-silver particle. B: Nano-silver solution. The average particle size of metallic silver in the nano-silver solution is about 20 nm, which has a broad-spectrum bactericidal effect and does not produce drug resistance.

### Observational Indices

In terms of recovery time, the time taken for erosion healing and improvement in patient eating were recorded for both groups. Additionally, the efficacy of the two groups was evaluated after treatment<sup>10</sup>. Inefficiency was recorded when the erosion and pain symptoms did not change or worsened and the exudation and congestion area did not decrease or increased. Improvement was recorded when the erosion and pain symptoms were relieved, and the area of exudation and congestion decreased <30%. The treatment was considered effective when the erosion and pain symptoms were significantly relieved, and the exudation and congestion area was reduced by 30%–60%. Significant effectivity was considered when the erosion and pain were basically relieved, and the exudated and congested area decreased >60% and <100%.

A visual analog scale (VAS) was used to assess

patient pain before treatment ( $T_0$ ) and at the 1st ( $T_1$ ), 3rd ( $T_3$ ), 5th ( $T_5$ ), and 7th ( $T_7$ ) day of treatment<sup>11</sup>. A scale plate with a scale of 0–10 cm was used to represent different degrees of pain, and the patients indicated the degree of pain themselves. The scale value matching the degree of pain was marked on the scale. 0 points meant painless, and 10 points meant severe pain. Evaluation of lesions: Oral lesions of patients were evaluated using the Reticulation/keratosis, erythema, and ulceration (REU) scoring system at time  $T_0$ ,  $T_1$ ,  $T_3$ ,  $T_5$ , and  $T_7$ , respectively. A full score was 3, 0 indicated no lesions, 1 indicated a lesion area <100 mm<sup>2</sup>, 2 indicated a lesion area of 100–300 mm<sup>2</sup>, and 3 indicated a lesion area >300 mm<sup>2</sup><sup>12</sup>.

Interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) were detected before and after treatment (the 8th day of treatment) to examine the levels of inflammatory cytokines. Samples of 5 mL of venous blood in a

fasting state were collected from the patients in the morning and centrifuged at 4,000 r/min for 10 min<sup>13</sup>. Enzyme linked immunosorbent assays (ELISAs) were used for determination. The ELISA instrument and kit were provided by Beijing Zhonghuitiancheng Technology Company.

Statistical Analysis Technique

The data from this study were quantified and analyzed using SPSS 19.0 software. Percentages (%) were compared using a  $\chi^2$  test. A chi-square value should be corrected when  $1 \leq$  theoretical frequency  $< 5$ . The measurement data were expressed as the mean  $\pm$  standard deviation. The recovery time and

inflammatory cytokine levels were compared using a t-test. The VAS score and REU score were compared by repeated measurement analysis of variance, and  $P < 0.05$  was considered statistically significant.

RESULTS AND DISCUSSION

Recovery and Effective Rate

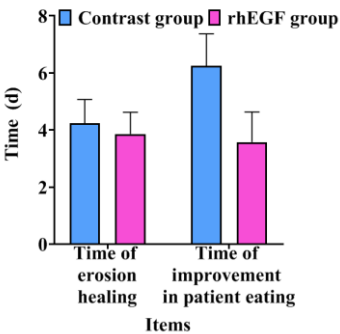
Compared with the contrast group, the times taken for erosion healing and improvement in patient eating were shorter in the rhEGF group patients (Table 2; Figure 4), and the total effective rate for these patients was higher ( $P < 0.05$ ; Table 3, Figure 5).

Table 2.  
Mean ( $\pm$  standard deviation) of recovery times of the two treatment groups

Group	Time of erosion healing (d)	Time of improvement in patient eating (d)
Contrast group (n = 60)	4.23 $\pm$ 0.84	6.24 $\pm$ 1.13
rhEGF group (n = 60)	3.86 $\pm$ 0.76	3.57 $\pm$ 1.06
t	2.530	13.350
P	0.013	< 0.001

Note. rhEGF: Recombinant human epidermal growth factor.

Figure 4.  
Recovery time.



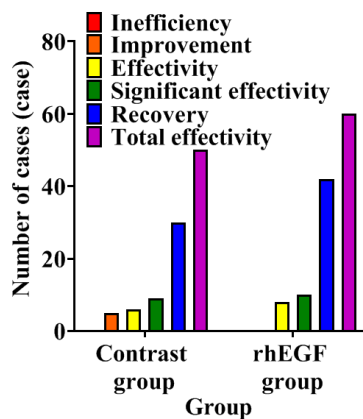
rhEGF: Recombinant human epidermal growth factor. The time taken for erosion healing and improvement in patient eating of rhEGF group patients were shorter, all  $P < 0.05$ .

Table 3.  
Comparison of the effectiveness of the two treatments.

Group	Inefficiency	Improvement	Effectivity	Significant effectivity	Recovery	Total Effectivity
Contrast group (n = 60)	0	5 (8.33)	6 (10.0)	9 (15.0)	30 (50.0)	50 (83.33)
rhEGF group (n = 60)	0	0	8 (13.33)	10 (16.67)	42 (70.0)	60 (100.0)
$\chi^2$						8.836
P						0.003

Note. rhEGF: Recombinant human epidermal

Figure 5.  
Curative effect.



rhEGF: Recombinant human epidermal growth factor. The total effective rate of the rhEGF group was higher,  $P < 0.05$ .

Visual Analog Scale and Reticulation/Keratosis, Erythema, and Ulceration Scores

The VAS and REU scores were lower in the rhEGF group than the contrast group, and all of the scores in both groups showed downward trends (Table 4 and 5, Figure 6). There were interaction

effects between the groups and time (VAS score:  $F_{\text{intergroup effect}} = 704.000$ ,  $F_{\text{time effect}} = 134.300$ ,  $F_{\text{interaction effect}} = 22.810$ . VAS score:  $F_{\text{intergroup effect}} = 1303.000$ ,  $F_{\text{time effect}} = 347.900$ ,  $F_{\text{interaction effect}} = 23.060$ . All  $P < 0.001$ ).

Table 4.  
Mean ( $\pm$  standard deviation) of the visual analog scale scores for the two treatments at different times.

Time	Contrast group (n = 60)	rhEGF group (n = 60)	t	P
T <sub>0</sub>	6.33 $\pm$ 0.65	6.43 $\pm$ 0.82	0.740	0.461
T <sub>1</sub>	5.32 $\pm$ 0.56	5.12 $\pm$ 0.80	1.586	0.115
T <sub>3</sub>	4.81 $\pm$ 0.56	3.45 $\pm$ 0.86	10.270	< 0.001
T <sub>5</sub>	3.42 $\pm$ 0.54	2.33 $\pm$ 0.77	8.977	< 0.001
T <sub>7</sub>	2.62 $\pm$ 0.49	1.88 $\pm$ 0.78	6.223	< 0.001

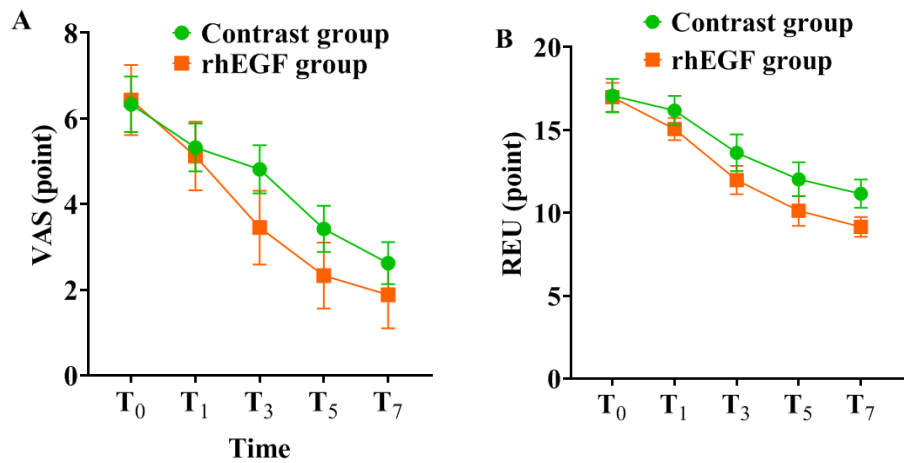
Note. rhEGF: Recombinant human epidermal growth factor. T<sub>0</sub>, T<sub>1</sub>, T<sub>3</sub>, T<sub>5</sub>, T<sub>7</sub> were before treatment and at the 1st, 3rd, 5th, and 7th day of treatment, respectively.

Table 5.  
Mean ( $\pm$  standard deviation) of the reticulation/keratosis, erythema, and ulceration scores at different times during the two different treatments.

Time	Contrast group (n = 60)	rhEGF group (n = 60)	t	P
T <sub>0</sub>	17.07 $\pm$ 1.01	16.97 $\pm$ 0.87	0.581	0.562
T <sub>1</sub>	16.17 $\pm$ 0.88	15.05 $\pm$ 0.67	7.844	< 0.001
T <sub>3</sub>	13.62 $\pm$ 1.11	11.97 $\pm$ 0.86	9.102	< 0.001
T <sub>5</sub>	12.02 $\pm$ 1.02	10.12 $\pm$ 0.90	10.820	< 0.001
T <sub>7</sub>	11.15 $\pm$ 0.85	9.15 $\pm$ 0.60	14.89	< 0.001

Note. rhEGF: Recombinant human epidermal growth factor. T<sub>0</sub>, T<sub>1</sub>, T<sub>3</sub>, T<sub>5</sub>, T<sub>7</sub> were before treatment and at the 1st, 3rd, 5th, and 7th day of treatment, respectively.

Figure 6.  
Visual analog scale (VAS) and reticulation/keratosis, erythema, and ulceration (REU) scores.



A: VAS score. B: REU score. T<sub>0</sub>, T<sub>1</sub>, T<sub>3</sub>, T<sub>5</sub>, and T<sub>7</sub> were before treatment and at the 1st, 3rd, 5th, and 7th day of treatment, respectively. The VAS score and REU score in the rhEGF group were lower than those in the contrast group,  $P < 0.05$ .

Inflammatory Cytokine Levels

Before treatment, there were no significant differences in the IL-1, IL-6, and TNF- $\alpha$  levels between the two groups ( $P > 0.05$ ). However, after

treatment, all of the inflammatory cytokine levels in the rhEGF group were lower than those in the contrast group ( $P < 0.05$ ) (Table 6, Figure 7).

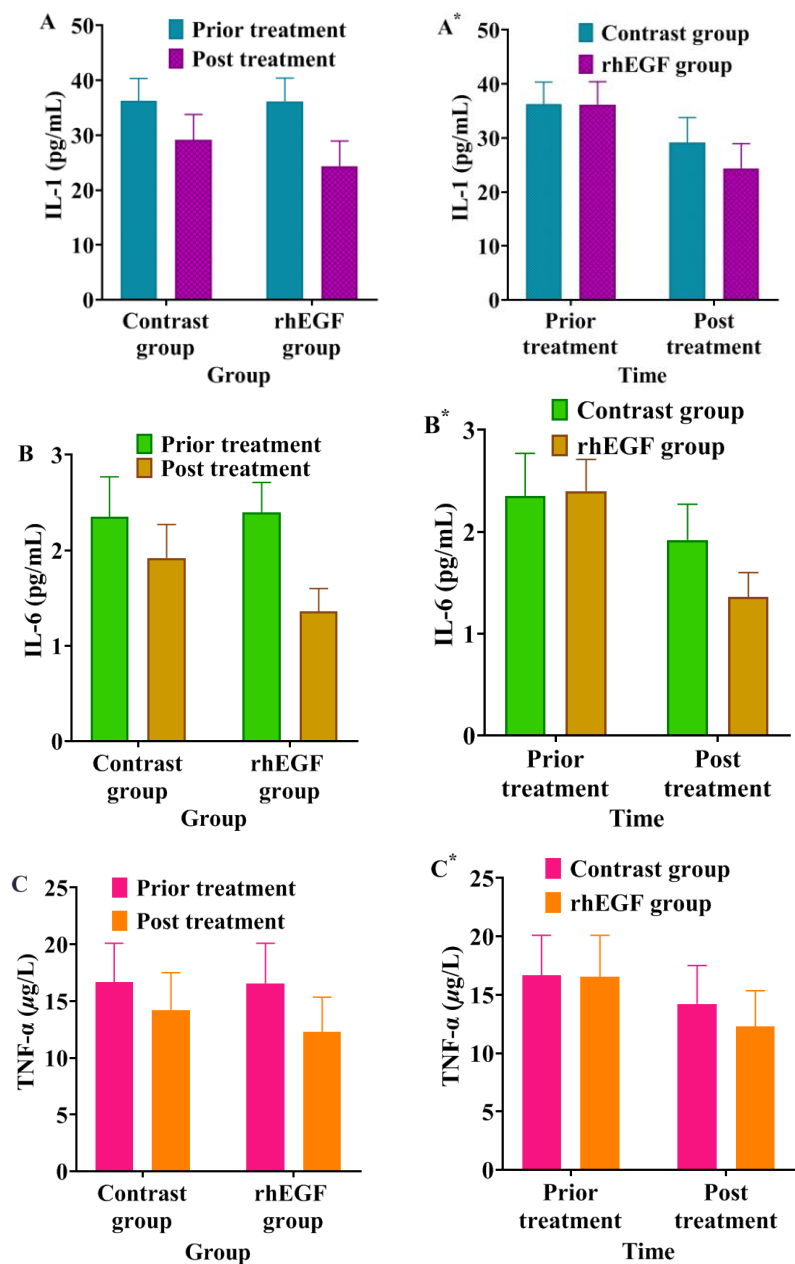
Table 6.  
Mean ( $\pm$  standard deviation) of inflammatory cytokine levels for the two treatments.

Time	Contrast group (n = 60)			rhEGF group (n = 60)		
	IL-1(pg/mL)	IL-6 (pg/mL)	TNF- $\alpha$ ( $\mu$ g/L)	IL-1 (pg/mL)	IL-6 (pg/mL)	TNF- $\alpha$ ( $\mu$ g/L)
Priortreatment	36.23 $\pm$ 4.11	2.35 $\pm$ 0.42	16.64 $\pm$ 3.45	36.16 $\pm$ 4.23*	2.40 $\pm$ 0.31*	16.57 $\pm$ 3.52*
Posttreatment	29.16 $\pm$ 4.62	1.92 $\pm$ 0.35	14.21 $\pm$ 3.29	24.37 $\pm$ 4.57*	1.36 $\pm$ 0.24*	12.28 $\pm$ 3.06*
t	8.856	6.092	3.948	14.670	20.550	7.125
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Note. The same index was compared between\* and the contrast group,  $P < 0.05$ . rhEGF: Recombinant human epidermal growth factor. IL-1: Interleukin-1, IL-6: Interleukin-6, TNF- $\alpha$  Tumor necrosis factor- $\alpha$



Figure 7.  
Inflammatory cytokines.



A, A\*: Interleukin-1 (IL-1); B, B\*: Interleukin-6 (IL-6); C, C\*: Tumor necrosis factor (TNF-α). All of the IL-1, IL-6, and TNF-α levels in the rhEGF group were lower than the values in the contrast group after treatment,  $P < 0.05$ .

Discussion

Oral mucosal erosion lesions is a common clinical disease of the oral mucosa. The erosion surface has no fixed shape, and it is red and smooth. Due to the absence of an epithelium layer, the tight blood vessels of connective tissue are exposed, resulting in friction between the mucous membranes in the mouth of the patient when eating or speaking, resulting in varying degrees of

pain. If the course of the disease is too long, then erosion symptoms can hide the original lesions, and there is also a risk of cancer<sup>14,15</sup>. Therefore, it is of vital to explore a timely and effective treatment for oral mucosal erosion lesions.

The results of this study showed that oral mucosal erosion wound healing was faster in patients treated with rhEGF gel, and their eating status improved earlier than patients treated with



ethacridine lactate. These results indicate that rhEGF gel effectively promoted wound tissue repair and wound healing through rhEGF. In this process, rhEGF activates cells and enables rapid synthesis of intracellular reproductive substances, such as hydroxyproline acid, DNA, and RNA, which strongly promote epithelial cell division and reproduction, accelerate the growth of granulation tissue on the eroding wound surface, and ultimately lead to early wound healing, so that patients can eat normally as soon as possible<sup>16,17</sup>.

The study also showed that rhEGF gel significantly reduced the VAS and REU scores for patients. The VAS score is a measure of pain, and the higher the score, the more severe the pain. The REU score is used to measure the oral lesions of patients. The higher the score, the larger the lesion area and the more severe the lesion. These results indicated that rhEGF gel had a good analgesic effect, and it could quickly reduce the scope of oral lesions<sup>18,19</sup>. Therefore, rhEGF gel should be applied to oral mucosal erosion lesions as soon as possible during treatment to supplement sufficient rhEGF to the wound to enable gene expression of the tissue cells in the area, ensure the continuous proliferation and differentiation of epidermal cells, and promote wound healing. IL-1, IL-6, and TNF- $\alpha$  are the main factors whose levels fluctuate substantially after inflammation occurs in the body, and their levels are abnormally elevated when inflammation occurs. Therefore, detecting their levels is essential for monitoring the development of inflammation in patients<sup>20</sup>. In this study, the levels of IL-1, IL-6, and TNF- $\alpha$  in patients treated with rhEGF gel were significantly lower than in those treated with conventional ethacridine lactate, suggesting that rhEGF gel has an advantage over conventional treatment in reducing the inflammatory response. Analysis suggests that rhEGF and EGF are similar in molecular structure and biological activity. Therefore, it combines with the corresponding receptors on the cell membrane surface and controls gene expression. In this way, it promotes the proliferation and growth of epithelial cells and the continuous removal of epithelial cells and fibroblasts from the wound. As a result, cell

metabolism is vigorous, and the degradation of collagen is reduced, reducing wound secretions and alleviating inflammation<sup>21-23</sup>.

Our results also showed that rhEGF gel used to treat patients in the observation period of total effective rate reached 100%, which is significantly higher than that of conventional treatment. rhEGF gel treatment enabled rapid wound healing, shortened the disease area, alleviated pain symptoms, and reduced inflammation in the patients. Eventually, it promoted patient recovery and improved treatment efficiency, which agrees with the results of other studies<sup>24</sup>. In addition to the application of rhEGF gel other nursing measures were also applied, including psychological support from nursing staff, and treatment assistance through the close cooperation of family members. These measures strengthened the confidence of the patients. Additionally, nursing staff also administered the required medication and an appropriate diet. This provided a solid foundation for the effective treatment of the oral mucosal erosion lesions. In terms of daily oral care, nano-silver was the main element of the nano-silver antibacterial mouthwash<sup>25,26</sup>. It can completely kill pathogenic bacteria, such as fungi, mold, *Escherichia coli*, and pyogenic bacteria in the oral cavity within 2 min. It is also suitable for daily oral health care and can prevent wound infection in patients with oral mucosa erosion lesions<sup>27</sup>. Therefore, it is beneficial to combine scientific and reasonable nursing measures in the treatment of oral mucosal erosion lesions<sup>28,29</sup>. A limitation of the study is that the sample size was limited. Therefore, the results could be biased. Further confirmation of our results is needed with larger and more reliable sample sizes.

## CONCLUSION

rhEGF promotes cell proliferation and differentiation by regulating the expression of genes in the wound tissue cells of patients with oral mucosa erosion lesions, enabling the rapid formation of oral mucosa epithelial cells. At the same time, rhEGF can significantly alleviate inflammation by inhibiting collagen degradation and reducing wound secretion. In this study,

patients with oral mucosal erosion lesions were divided into two groups that were treated with ethacridine lactate or rhEGF gel, and all patients received nursing measures. The analysis found that patients treated with rhEGF gel had lower VAS scores, REU scores, and inflammatory cytokine levels than patients treated with conventional ethacridine lactate. Additionally, they had a higher total effective rate (up to 100%), shorter recovery time, and improved eating time during the observation period. The results showed that the pain, oral lesions, and inflammation of patients treated with rhEGF gel were significantly reduced, and all patients in this group received effective treatment. These findings indicate that rhEGF gel had a significant and rapid wound healing effect on the treatment of oral mucosal erosion lesions. Therefore, rhEGF gel has a high clinical application value.

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