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A Study on the Mechanisms by Which AGEs and RAG Promote Wound Healing in Patients with Second-Degree Burns undergoing Eschar Grinding Combined with Drug Therapy

Weijie He[1], Zhi Liu[2], Lujun Yang[1], Sitian Xie[1], Zhan Ouyang[1], Yao Lin[1], Fuhua Huang[1], Shijie Tang[1*]

[1]Second Affiliated Hospital of Shantou University Medical College, Shantou, China
[2]Shiquan County Hospital, Ankang City, Shaanxi Province, Ankang, China
Email: 185684815@qq.com, 147658802@qq.com, sitianx@163.com, ouyang0600@163.com, 1026977140@qq.com, *sjtang3@stu.edu.cn

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Abstract

Objective: To evaluate the improvement effect of combined treatment of eschar abrasion, nanosilver dressing, and mussel mucin spray on wound healing in patients with second-degree burns, and to explore their effects on the expression level of (advanced glycation end products) AGEs in wound tissue, so as to provide a basis for the application of AGEs expression level in wound tissue in the future clinical treatment of second-degree burns. **Methods:** Patients with second-degree burns admitted to the Department of Burns and Plastic Surgery of the Second Affiliated Hospital of Shantou University Medical College from July 2023 to July 2024 were selected as the research subjects. This study was a non-double-blind study, and both patients and researchers were aware of the treatment methods. They were randomly divided into Group A (control group) and Group B (study group). According to the order of their visits, the patients were numbered in advance; then the seed number was taken, and 70 random numbers were generated on the computer using SAS, the first 35 corresponding to group A, and the last 35 corresponding to group B; the random numbers were arranged from small to large, and the rank of the random numbers was the patient number; finally, the patient numbers were arranged from small to large, and the corresponding groups were the grouping scheme. 1) Wound healing time: The wound healing was observed every day, and the wound healing time was calculated when the wound was completely epithelialized. 2) Wound healing: The wound healing area was measured 1, 7, and 14 days after treatment, and transparent paper was used to

record combined with a computer-assisted imaging system. Wound healing rate = wound healing area (cm^2)/total wound area before treatment (cm^2) × 100%. The time for complete wound healing was recorded in the two groups of patients. 3) Pain: The pain was evaluated at 1, 7, and 14 days after treatment using the visual analogue scale (VAS). The higher the score, the more severe the pain. 4) Scar condition: Scar formation was evaluated 1, 3, and 6 months after wound healing using the VAS scale, with a total score of 15 points. The higher the score, the more severe the scar. 5) Detect the expression of AGEs in wound tissue. **Results:** The wound healed 14.03 ± 2.28 days after eschar removal, with a cure rate of 97.8%. No infection occurred in the wound after eschar removal in all patients. The wound healing time ranged from 9 to 23 days, with an average healing time of 28.41 ± 1.45 days. The healing quality was satisfactory. The Vancouver Scar Scale scored the wound healing scar as 0.81 ± 0.73 points. Western blot was used to detect the expression of AGEs, (receptor for advanced glycation end products) RAGE, and protein in the wound tissue. Results After 7, 14, and 28 days of medication, the wounds of diabetic patients healed well. The drug treatment efficacy and hydroxyproline content showed an upward trend, and the expression levels of AGEs, RAGE, and HIF-1a proteins showed a downward trend. Compared with day 0, the hydroxyproline content of the wound granulation tissue on days 7, 14, and 28 was significantly increased (P≪ 0.01), and the expression levels of AGEs, RAGE, and HIF-1*α* proteins were significantly downregulated (P≪ 0.05 or P≪ 0.01). **Conclusion:** Monitoring the expression levels of AGEs and RAGE can reflect the wound-healing effect of patients with second-degree burns, and the prognosis of the wound is closely related to the expression levels of AGEs, RAGE, and scab abrasion. In the treatment of second-degree burn wounds, scab abrasion can grasp the level of necrotic scab removal, can achieve "relatively accurate" removal of necrotic tissue, maximally protect the ecological tissue between wounds and retaining normal tissue, and can play a positive role in promoting the healing process of burn wounds; at the same time, nanosilver dressings have good antibacterial properties and high safety, and mussel mucin has anti-inflammatory and antioxidant activities and the characteristics of blocking nerve endings, which can effectively relieve the burning, stinging, and itching of sensitive skin and effectively promote wound healing.

Keywords

AGEs, RAG, Dermabrasion, Second Degree Burns

1. Introduction

Burns are a relatively serious accidental trauma in people's daily production and life. Among all traumas, the mortality rate of accidental incidents caused by burns ranks fourth [1]. Second-degree burns can be divided into two types. One is superficial second-degree burns, which are mainly manifested by skin flushing, large

blisters, severe pain, and red wounds after skin damage. The other is deep second-degree burns, which are mainly manifested by small blisters, red and white wounds after skin damage, and severe pain. Epidemiological studies have shown [2]. In clinical practice, the wounds of hospitalized patients with burns and scalds are mostly deep second degree. The pathological characteristics are that the injury layer mainly involves the entire epidermis and the papillary dermis, while the reticular dermis is less damaged, and there are still a considerable number of undamaged hair follicles, sweat glands, sebaceous glands and other skin appendages. These skin appendages contain a certain amount of epithelial cells, which can proliferate and crawl under suitable conditions to cover the wound surface [3]. The high sugar environment in the body of patients with second-degree burns and the accumulation of advanced glycation end products (AGEs) in the epidermal tissue can lead to abnormal function of epidermal tissue cells or matrix. Disorders in sugar metabolism can lead to the local accumulation of a large number of AGEs, which is an important pathological basis for damage to multiple tissues and organs such as skin nerves and blood vessels [4]. The receptor of Advanced Glycation Endproducts (RAGE) is only expressed in small amounts on endothelial cells. In a high-sugar environment, as the production and accumulation of AGEs due to glucose metabolism disorders increases, RAGE expression increases. AGEs change the function of endothelial cells through the RAGE pathway. AGEs can also affect the proliferation function of fibroblasts. By inducing high expression of inflammatory factors in the wound and inhibiting their ability to synthesize collagen, wound repair is always in the inflammatory response stage, delaying wound healing. Therefore, the expression levels of AGEs and RAGE can reflect the wound healing effect of patients with II degree burns.

If appropriate treatment options are chosen early to treat second-degree burn wounds, on the one hand, the degree of wound infection can be reduced and progressive deepening can be avoided; on the other hand, the epithelial tissue in the remaining appendages of the dermis that has not been destroyed by early injury factors and later infection factors can continue to proliferate and crawl, forming many "skin islands" on the wound surface, which can shorten the wound healing time, reduce the degree of scar hyperplasia in the later stage, and improve the patient's prognosis [5] [6]. However, if the early treatment measures for the wounds of patients with second-degree burns are inappropriate, the wound infection will worsen, and the still viable dermis and its inner skin appendages will further necrotize, causing the wound to progressively deepen to a deeper level, which will have an adverse effect on the patient's prognosis [7] [8]. Therefore, how to treat second-degree burn wounds in the early stage is of great significance to the patient's prognosis.

Ecstatic abrasion was the earliest surgical method used to treat deep burn wounds and once became the preferred method for treating deep second-degree burn wounds [9]. However, due to the dynamic, three-dimensional, and uneven characteristics of second-degree burn wounds, it is difficult to determine the appro-

priate level of necrotic scab removal during surgery, making it impossible to ensure the effectiveness and controllability of removing necrotic tissue. Although escharectomy has been used clinically for many years, there are still significant differences in the timing, instruments, steps, postoperative dressing selection, and postoperative dressing change methods of this procedure among different institutions, resulting in uneven clinical results [10].

For patients with second-degree burns, successful surgery is only the basis for the patient's recovery. In addition to systemic nutritional support therapy, wound dressing treatment after surgery will also directly affect the patient's recovery. In the past clinical treatment, simple vaseline gauze combined with gauze cotton pads and elastic bandages were mostly used for bandaging after surgery [11]. However, combined with the actual results, it was found that the wound healing speed of this treatment method is very slow and it is prone to serious infection [12]. Therefore, new and truly effective postoperative dressings have become an urgent clinical need. When selecting external dressings for postoperative wounds, first of all, they must have good biocompatibility with the wound surface, and secondly, they must have a barrier function to protect the wound surface and reduce exudation. At the same time, it must be able to effectively resist various microorganisms, resist infection, and ultimately promote skin tissue repair and functional recovery [13] [14].

In recent years, more and more new multidrug-resistant bacteria have emerged, and traditional silver ion antibacterial preparations cannot fully meet clinical requirements. Nanosilver dressings contain nanosilver ions, which have strong broad-spectrum antibacterial effects and can quickly release nanosilver ions. Nanosilver ions can quickly kill pathogenic microorganisms such as fungi and bacteria [15], and have good air permeability, which can help clean wounds, keep wounds moist for a long time, and help relieve wound pain and shorten wound healing time [16]. According to current domestic and foreign literature research, the use of nanosilver dressings alone can significantly reduce the infection rate of wounds [17] [18]. However, its efficacy in combination with other drugs needs further study. This study used mussel mucin spray, whose main ingredient is a protein purified from the foot gland of marine blue mussels. Because the spray is rich in lysine and has a high positive charge load at normal pH, it plays an important role in biological connection, forming a protective film, and promoting cell adhesion and crawling [19]. At the same time, in recent years, more and more scholars have found that it can effectively reduce scar itching during burn healing without causing skin irritation and allergies, and has no dependence [20]. This study observed the clinical effect of the combined treatment of eschar removal and mussel mucin spray, explored the effect on the expression of AGEs and RAGE in wound tissue, and provided a reference for the clinical treatment of second-degree burns.

The stress response of patients after burns can improve their ability to adapt to changes in the internal and external environments, which is beneficial to main-

taining the homeostasis of the internal environment. However, an overly strong stress response of the body can easily lead to many adverse consequences, such as reactive hyperglycemia, which is extremely detrimental to the rehabilitation of patients with second-degree burns [21]. Patients with second-degree burns not only face the difficulty of shock caused by fluid loss, but also face the risk of infection due to damage to the skin and mucosal barrier. Patients with deep burns also need scab removal and multiple skin grafts, and rehabilitation treatment is required after discharge to restore normal limb function [22] [23].

After burns, patients are in a state of stress, and many systems of the body will change to participate in the formation of stress-induced hyperglycemia, mainly changes in the neuroendocrine system, changes in the concentration of various cells and inflammatory factors, and increased insulin resistance in peripheral cell tissues [24]. After burns, the excitability of the sympathetic system increases, and the secretion and release of catecholamines (epinephrine and norepinephrine) synthesized in the adrenal medulla controlled by the sympathetic nerves will increase. These two hormones are the main hormones that increase after stress in the body [25]. Catecholamines mainly bind to the body's α and β receptors to produce corresponding physiological effects. After the body is subjected to burn stress, catecholamines bind more to pancreatic B cell α receptors, resulting in decreased insulin secretion; at the same time, adrenaline also excites pancreatic A cells, increasing their secretion of glucagon. In addition to acting on the pancreas as a target organ, elevated catecholamines also act on other target organs such as the liver, increasing their glycogenolysis and gluconeogenesis [26] [27].

At the same time, the high sugar environment in the body of patients with second-degree burns and the accumulation of advanced glycation end products (AGEs) in the epidermal tissue lead to the inability of epidermal tissue cells or matrix to function normally [28]. Disorders in glucose metabolism lead to the local accumulation of a large number of AGEs, which is an important pathological basis for damage to multiple tissues and organs such as skin, nerves and blood vessels [29]. Under normal circumstances, the receptor of advanced glycation end products (RAGE) is only expressed in small amounts on endothelial cells. In a high-sugar environment, as the number of AGEs produced and accumulated by glucose metabolism disorders increases, RAGE expression increases accordingly. AGEs change the function of endothelial cells through the RAGE pathway.

AGEs can also affect the proliferation function of fibroblasts. By inducing high expression of inflammatory factors in the wound surface and inhibiting its ability to synthesize collagen, wound repair is always in the inflammatory response stage, which will delay wound healing [30]. Studies have confirmed that AGEs exert their biological effects mainly through non-receptor pathways (direct damage) and receptor pathways. Receptor pathway: AGEs interact with the receptor RAGE present on the endothelial cell membrane, and a series of receptor signal transduction pathways are activated, leading to the formation and release of multiple cytokines and causing pathological changes in the body's blood vessels and nerves

[31]. Non-receptor pathway: AGEs change their structure and function by directly modifying proteins, lipids, nucleic acids, etc. Among them, the main pathway of AGEs is the receptor pathway, which plays a more important role in the damage caused by AGEs [32]. Therefore, monitoring the expression levels of AGEs and RAGE can reflect the wound healing effect of patients with second-degree burns.

The principle of eschar abrasion is based on the friction or dermabrasion that was first developed in plastic surgery. It refers to the use of the shear force generated by the friction instrument to remove part of the diseased skin tissue, form a fresh wound in the middle of the normal skin tissue, and stimulate the remaining epithelium in the base of the wound and the healthy tissue at the edge to crawl and heal again, thereby achieving the purpose of removing the diseased tissue and improving the appearance of the skin. The eschar abrasion used for burn wounds also uses the shear force generated by the repeated friction of the rough surface of the eschar abrasion tool in the horizontal direction of the wound to remove the necrotic tissue in the wound layer by layer, which can maximize the preservation of the undamaged dermis and the skin appendages inside it [33]. When the wound tissue has dense pinpoint bleeding or the tissue turns red, it is the appropriate level after the eschar is removed. Compared with eschar cutting, eschar abrasion makes it easier to grasp the level of necrotic eschar removal, can achieve 'relatively precise' removal of necrotic tissue, and maximize the protection of the ecological tissue between the wound and the preservation of normal tissue. It can play a positive role in promoting the healing process of burn wounds [34]. The disadvantage of eschar abrasion is that the medical expenses are high and it has strict indications.

Under normal circumstances, after eschar abrasion, patients with second-degree burns are usually treated with repeated dressing changes using vaseline gauze combined with gauze pads and elastic bandages. This treatment has limited anti-infection effects and cannot promote wound healing. Most importantly, when changing the dressing, the wound will be stretched to destroy the new granulation tissue, which will directly lead to delayed healing [35] [36] and increase the pain of the patient. Therefore, changing the dressing used for long-term dressing changes after surgery is the general trend in clinical practice to completely cure second-degree burns. Current studies at home and abroad have shown [37] that nanosilver dressings have good antibacterial properties and high safety, but they are powerless to promote tissue regeneration and various discomforts during scar formation. Therefore, the use of nanosilver dressings alone has certain limitations [38].

Mussel mucin spray comes from the marine invertebrate mussel. Scientists have purified a protein called mussel mucin from the foot gland of mussel. It has the functions of accelerating wound healing, forming a protective film and relieving itching and bleeding. It has a good affinity with the human body, is highly safe, has no toxic side effects, and is not dependent [39]. The disadvantage of mussel mucin spray is that some patients may experience side effects. It has a relatively

strict indication for use. Patients should pay attention to their diet and clothing during medication. The general mechanism of action of mussel mucin spray is: 1) Mussel mucin contains a lot of alkaline protein lysine, and its isoelectric point is pH9.5. Under normal physiological conditions, it has a high load of positive charge and attracts various negatively charged normal epidermal cells, endothelial cells, fibroblasts, etc., from the periphery or bottom of the wound to the center of the wound by electrostatic action. It also generates an electronic current conduction signal by forming a potential difference between cells to maintain the potential balance between healthy cells and damaged cells, so that the diseased cells can be effectively restored, thereby truly accelerating wound healing; 2) The content of L-Dopa in mussel mucin is relatively high. This group has excellent anti-inflammatory and antioxidant activity. Oxidized DOPA and unoxidized DOPA cross-link to form a polymer, which completely fixes the mucin on the tissue surface. In addition, this group can bind to the receptors of the skin nerve endings to block the ends and relieve itching. 3) Patients with third-degree burns use mussel mucin spray after debridement, eschar excision and skin grafting. As the water in the spray evaporates, a breathable, transparent and elastic biofilm will form on the wound surface and last for a long time. It can not only exert the above effects for a long time, but also resist the invasion of various pathogenic microorganisms [40] [41].

Some scholars have compared the clinical efficacy of traditional iodine dressings and new nanosilver dressings. They found that nanosilver dressings can dilate blood vessels and improve local blood circulation [42]. Some scholars have also pointed out that the use of mussel mucin in the healing of incisions in minimally invasive spinal surgery has significantly improved the grade A healing rate of incisions, and significantly shortened the healing time and hospitalization time [43]. Literature reports that nanosilver dressings were used on chronic wounds infected with fungi. Scholars placed nanosilver in a solution to study its effects on multidrug-resistant bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. They found that nanosilver can not only kill these common bacteria in a targeted manner, but also has excellent inhibitory effects on fungi and multidrug-resistant bacteria [44]. Some scholars have conducted a series of experiments on mussel mucin-related products on sensitive facial skin and found that mussel mucin can significantly relieve the burning, stinging, and itching sensations of sensitive skin. They believe that the efficacy is due to the excellent anti-inflammatory and antioxidant activity of mussel mucin itself and its ability to block nerve endings [45].

In the past, there were many clinical reports on the treatment schemes and effects of patients with second-degree burns, but most of them were single eschar abrasion combined with conventional drugs, and there was a lack of relevant studies on the efficacy of eschar abrasion, nanosilver dressings, and mussel mucin spray combined to treat second-degree burns. In this context, in this study, we innovatively evaluated the wound healing and AGEs expression levels in wound tissue of patients with second-degree burns treated with eschar abrasion, nanosil-

ver dressings, and mussel mucin spray, in order to compare the improvement of different treatment schemes on the wound healing process and AGEs expression levels in wound tissue of second-degree burns. The improvement effect of eschar abrasion, nanosilver dressings, and mussel mucin spray on wound healing of patients with second-degree burns was further clarified, and its effect on the expression level of AGEs in wound tissue was explored, in order to provide a basis for the application of AGEs expression levels in wound tissue in the future clinical treatment of second-degree burns. At the same time, relevant suggestions were put forward based on the research results, which was also lacking in previous studies and can provide guidance for the clinical treatment of patients.

2. Research Methods

Patients with second-degree burns admitted to our burn and plastic surgery department from July 2023 to July 2024 were selected as research subjects.

3. Inclusion Criteria

1) The patient had a clear history of thermal injury, and according to China's "four-degree five-point method", the wound depth was determined to be second degree (confirmed by two senior attending physicians and above), and skin blisters. The bottom of the blister was red or white and filled with clear, viscous liquid. It was sensitive to touch and turned white when pressed;

2) Aged 18 to 60 years old, without diabetes, heart disease and other diseases that seriously affect wound healing;

3) The patient's information was complete, compliance and surgical tolerance were good, and he could cooperate to complete treatment and follow-up.

4. Exclusion Criteria

- Severe shock symptoms at admission, shock index > 2. Shock index = heart rate/systolic blood pressure, less than 0.5 is normal, 0.5 - 1 is mild shock, 1 - 1.5 is moderate shock, 1.5 - 2 is severe shock, and greater than 2 is severe shock.
- Combined with severe infection, systemic sepsis, or combined with systemic multiple organ failure;
- Combined with other severe complex injuries, requiring specialist treatment;
- Combined with moderate to severe inhalation injury;
- Patients with chemical burns;
- Combined with other congenital diseases;
- Combined with heart, lung, liver, kidney and other visceral organ dysfunction, requiring special intervention treatment;
- Combined with chronic underlying diseases such as diabetes, coronary heart disease;
- Patients who have been using hormones or immunosuppressants for a long time before injury;
- Patients who are pregnant or breastfeeding.

5. Sample Size and Grouping

Sample size calculation formula:

u^{α}—the u value corresponding to the test level α

u^{β}—the u value corresponding to the type II error probability β;

δ—the difference between the two population means, $\delta = \mu 1 - \mu 2$;

σ—population standard deviation.

The bilateral α is 0.05, and β is 0.1. The table shows $u0.05/2 = 1.96$, $u0.1 = 1.282$. Wound healing is used as the effect index. According to relevant literature and previous studies [44], $\delta = 7.31$, $n1 = n2 = 45$, $S1 = 9.72$, $S2 = 5.77$, and $\sigma = 8.79$ is obtained. The sample size of each group is calculated to be 31 cases. Based on the dropout rate of 10%, about 35 patients are included in each group, for a total of 70 patients.

6. Grouping

This study is a non-double-blind study, and both patients and researchers are aware of the treatment methods. The patients were randomly divided into Group A (control group) and Group B (study group). The specific method is as follows: First, the patients were numbered in advance according to the order in which they visited the hospital; then the seed number was taken, and SAS was used to generate 70 random numbers on the computer. The first 35 corresponded to Group A, and the last 35 corresponded to Group B; the random numbers were arranged from small to large, and the rank of the random numbers was the patient number; finally, the patient numbers were arranged from small to large, and the corresponding groups were the grouping scheme.

7. Intervention Method

Control group measures: Abrasions were used for treatment. The operation was generally performed within 48 to 72 hours after injury. After admission, the patient received standardized fluid resuscitation treatment. The vital signs such as body temperature, blood pressure, respiration, pulse, and blood oxygen saturation were stable, and the urine volume was maintained at 60 to 100 ml/h. The anesthesiologist assessed that the patient could tolerate general anesthesia, and abrasion was performed on the burn wound. After general anesthesia, the patient was cleaned with hydrogen peroxide and saline three times alternately, and the surgical area was routinely disinfected with iodine. The surgeon rubbed the wound repeatedly with medical metal steel wool, and the assistant rinsed the rubbed wound with saline to remove blood stains and facilitate the judgment of the depth of abrasion. The surgeon judged the surgical level while abrading the scab until dense pinpoint bleeding or redness was visible on the wound. Use normal saline to carefully rinse the wound three times again. After careful hemostasis, cover it with vaseline gauze and a thick gauze cotton pad and apply pressure with an elastic bandage. According to the penetration of the outer dressing, the dressing is usually changed for the first time on the 2nd to 3rd day after surgery. If the wound

exudates little, there is no abnormal secretion, and the inner dressing adheres well, the inner dressing can be retained and only the outer dressing can be changed; if the wound exudates a lot, or there is abnormal secretion, and the inner dressing adheres poorly, the inner dressing needs to be changed at the same time. Change the dressing regularly according to the dressing change standards until the wound heals.

The measures of the research group were combined treatment with abrasion, nanosilver dressing, and mussel mucin spray. The surgical method was the same as that of the control group. 3 ml of mussel mucin spray was evenly sprayed on the wound surface, and then covered with a 20 × 25 cm nanosilver dressing and a thick gauze cotton pad, and finally bandaged with an elastic bandage. Then the dressing was changed regularly according to the exudation of the wound, and the exudate and secretions were handled in time, and the necrotic small skin flakes were removed at the same time. The dressing change criteria: the outer dressing was penetrated, the patient was in obvious pain, and the dressing in the surgical area had a distinct odor.

8. Monitoring Indicators and Data Collection

In order to prevent information bias caused by data collection, the personnel involved in this research project will be systematically trained before the experiment begins, so that they can master the experimental plan and evaluation criteria; all data will be collected by specially trained researchers. Data collection will be carried out separately to avoid mutual prompts affecting the results.

9. Observation Indicators

- Wound healing time: Observe the wound healing situation every day. When the wound is completely epithelialized, calculate the wound healing time.
- Wound healing situation: Measure the wound healing area 1, 7, and 14 days after treatment, using transparent paper tracing combined with computer-assisted imaging system. Wound healing rate = wound healing area (cm^2)/total wound area before treatment (cm^2) × 100%. Record the time when the wound is completely healed in both groups of patients.
- Pain: Evaluate the pain 1, 7, and 14 days after treatment using the visual analogue scale (VAS). The higher the score, the more severe the pain.
- Scar situation: Evaluate the scar formation 1, 3, and 6 months after wound healing using the VAS scale, with a total score of 15 points. The higher the score, the more severe the scar.
- Detect the expression of AGEs in wound tissue

10. Experimental Detection Method and Principle

10.1. ELISA Method

Take part of the wound tissue, rinse it in ice water, wipe it dry, weigh it, cut it into pieces, prepare 10% tissue homogenate at a volume of 1:9 0.9% sodium chloride

solution, and determine the total protein quantification by BCA method. The homogenate is centrifuged at 3000 r/min for 10 minutes, with a centrifugal radius of 15 cm, and the supernatant is taken. The ELISA kit is equilibrated at room temperature for 60 minutes. According to the instructions of the ELISA kit, set up standard wells and sample wells, add 50 μL of different concentrations of standard wells to each standard well; add 10 μL of the sample to be tested to the sample well first and then add 40 μL of sample diluent; then add 100 μL of horseradish peroxidase (HRP) labeled detection antibody to each well of the standard well and sample well, seal the reaction well with a sealing film, and incubate in a 37˚C constant temperature box for 60min. Discard the liquid, pat dry on absorbent paper, fill each well with washing solution (20× washing buffer dilution: distilled water diluted 1:20) and let stand for 1min; shake off the washing solution, pat dry on absorbent paper, and repeat the washing plate 5 times. Add 50 μL of substrate A and B to each well and incubate at 37˚C in the dark for 15 min. Add 50 μL of stop solution to each well, and within 15 min, use a full-wavelength automatic multifunctional microplate reader to measure the OD value of each well at a wavelength of 450 mm.

10.2. Experimental Principle

Total protein quantitative test (BCA method) Principle: BCA method is an ideal protein quantitative method. In an alkaline environment, the peptide bond structure in the protein molecule complexes with Cu^{2+} and reduces Cu^{2+} to Cu^{+}. BCA specifically binds to Cu^{+} to form a stable purple-blue complex, with the maximum light absorption value at 562 nM and is proportional to the protein concentration. The depth of the color is proportional to the protein content. According to the proportionality between absorbance and concentration, the concentration of the protein to be tested can be calculated by measuring the absorbance. Calculation formula: Total protein concentration (μg/ml) = (measured OD value-blank OD value/standard OD value-blank OD value) × standard concentration sample (563 μg/mL) × pre-test dilution multiple. This determination method has high sensitivity and is a simple operation. The reagents and the color complexes formed are both stable and are less affected by interfering substances such as detergents. Principle of ELISA kit: The kit uses double antibody sandwich enzyme-linked immunosorbent assay (ELISA). Into the coated microwells pre-coated with human advanced glycation end products (AGEs) and human advanced glycation end product specific receptor (RAGE) capture antibodies, the specimen, standard, and HRP-labeled detection antibody are added in turn, incubated and thoroughly washed. The substrate TMB is used for color development. TMB is converted into blue under the catalysis of peroxidase and into the final yellow under the action of acid. The depth of color is positively correlated with the human advanced glycation end products (AGEs) and human advanced glycation end product specific receptor (RAGE) in the sample. The absorbance (OD value) is measured at a wavelength of 450 nm using an enzyme reader to calculate the sample concentra-

tion.

10.3. Statistical Analysis

SPSS 20.0 was used for statistical analysis. $P < 0.05$ was considered statistically significant for two-sided tests.

1) General data: Quantitative data were expressed as mean ± standard deviation (normal distribution) or median/quartile (skewed distribution); count data were expressed as frequency and percentage.

2) Comparison between the intervention group and the control group at baseline and after intervention: Quantitative data were analyzed by t-test of two independent samples (normal distribution) or nonparametric rank sum test (skewed distribution); count data were analyzed by chi-square test.

All data of burn patients were tested using SPSS20.0 software. Continuous qualitative data of clinical indicators and quality of life of burn patients were expressed as ($x \pm s$). Quantitative data of treatment effect and complication rate were expressed as [n/(%)] and subjected to χ^2 test. $P < 0.05$ indicated that the difference was statistically significant. (Tables 1-3)

Table 1. Analysis of therapeutic effect [n/(%)].

Group	Significant effect	Effective	Invalid	Efficiency
Control group (n = 35)	15 (30.00)	26 (52.00)	9 (18.00)	41 (82.00)
Observation group (n = 35)	20 (40.00)	28 (56.00)	2 (4.00)	48 (96.00)
χ^2	----	----	----	5.005
P	----	----	----	0.025

Table 2. Analysis of clinical indicators ($x \pm s$).

Group	Hospitalization time (d)	Pain score	Wound healing time (d)
Control group (n = 35)	17.84 ± 1.33	5.71 ± 0.76	28.41 ± 1.45
Observation group (n = 35)	11.64 ± 2.55	2.99 ± 0.47	14.03 ± 2.28
t	13.060	12.687	6.591
P	<0.001	<0.001	<0.001

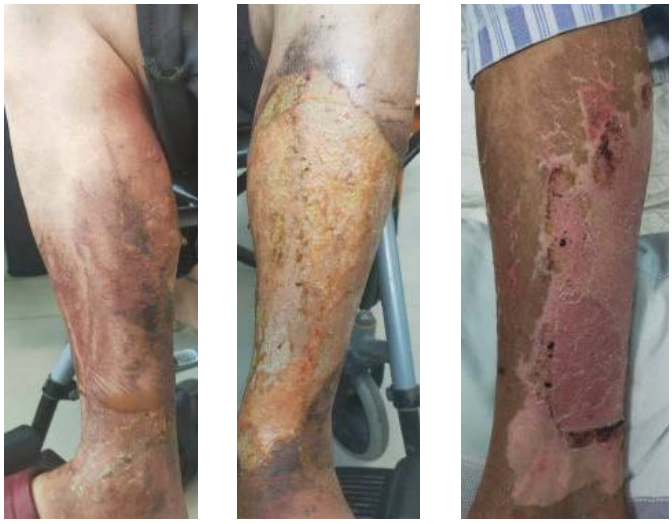
Table 3. Analysis of the incidence of complications [n/(%)].

Group	Infection	Inhalation injury	Shock	Stress ulcer	Incidence rate (%)
Control group (n = 35)	3 (6.00)	1 (2.00)	1 (2.00)	2 (4.00)	7 (14.00)
Observation group (n = 35)	1 (2.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (2.00)
χ^2	----	----	----	----	4.891
P	----	----	----	----	0.026

11. Results

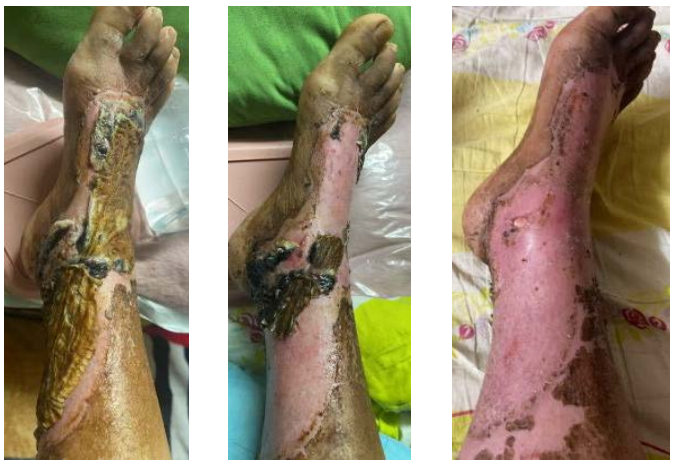
In the observation group, the scabs on the wound surface gradually softened after

4 days of treatment, and the fiber cords connected to the base became less; after 6 days of treatment, most of the scabs slowly fell off; after 8 days of treatment, the scabs on the wound surface of the patients were basically dissolved, the base was bright red, the deep granulation tissue increased rapidly, and the epithelialization near the wound edge was obvious. Typical case pictures are shown in Figure 1 and Figure 2.



(1 d) (7 d) (14 d)

Figure 1. Male patient, 67 years old, comparison of wound healing at 1 day, 7 days, and 14 days after deep second burn.



(1 d) (7d) (14 d)

Figure 2. Female patient, 65 years old, comparison of wound healing at 1 day, 7 days, and 14 days after deep second burn.

In the control group, dry scabs formed on the wound surface and necrotic tissue on the base after 4 days of treatment; after 6 days of treatment, the wound surface of the patients was relatively dry, and some yellow-white necrotic tissue turned yellow-black, and the necrotic tissue had not fallen off; after 8 days of treatment,

the dry scabs on the wound surface of the patients gradually softened; after 10 days of treatment, the base granulation tissue grew and the dry scabs slowly fell off.

Comparison of VAS scores before and after treatment between the two groups

Before treatment, there was no significant difference in VAS scores between the two groups ($P > 0.05$);

After treatment, the VAS scores of the two groups were significantly lower than those before treatment ($P < 0.01$), and the observation group was significantly lower than the control group ($P < 0.01$).

Comparison of scab lysis rates between the two groups

The scab lysis rates of the observation group were significantly higher than those of the control group at 1 week and 2 weeks of treatment ($P < 0.01$); the scab lysis rates of the two groups were 100% at 3 weeks and 4 weeks of treatment.

Comparison of complete scab dissolution time and wound healing time between the two groups

The complete scab dissolution time and wound healing time of the observation group were significantly shorter than those of the control group ($P < 0.01$).

Comparison of AGEs, RAGE, expression

There was no significant difference in the expression levels of AGEs, RAGE, and in the wounds of the two groups before treatment ($P > 0.05$); compared with before treatment, the expression levels of AGEs, RAGE, and in the two groups of patients decreased significantly after 2 weeks of treatment, and the expression levels of AGEs, RAGE, and in the observation group were significantly lower than those in the control group ($P < 0.01$).

Comparison of safety between the two groups

One patient in the control group felt a burning sensation subjectively, which was relieved after 30 minutes. No allergic reaction occurred in the two groups of patients. No adverse reactions related to drugs were found in the blood routine examination of the two groups of patients.

The cure rate after eschar removal was 97.8%. No infection occurred in the wound after eschar removal in all patients. The wound healing time was 9 to 23 days, with an average healing time of 28.41 ± 1.45 days. The healing quality was satisfactory. The Vancouver Scar Scale scored 0.81 ± 0.73 points for wound healing. Western blot was used to detect the expression of AGEs, RAGE, and protein in the wound tissue. Results After 7, 14, and 28 days of medication, the wounds of diabetic patients healed well. The drug treatment efficacy and hydroxyproline content showed an upward trend, and the expression levels of AGEs, RAGE, and HIF-1a proteins showed a downward trend. Compared with day 0, the hydroxyproline content of the wound granulation tissue on days 7, 14, and 28 was significantly increased (P< 0.01), and the expression levels of AGEs, RAGE, and HIF-1α proteins were significantly downregulated (P≪ 0.05 or P≪ 0.01).

12. Discussion

The focus of deep second-degree burn treatment is to avoid infection and promote

the repair or regeneration of residual skin tissue. The healing of burn wounds requires the participation of multiple cytokines, among which epidermal growth factor, which promotes the mitosis of multiple cells, plays an important role. Recombinant human epidermal growth factor gel preparations are developed by gene recombination technology. They can not only promote cell proliferation and division, but also promote the growth of granulation tissue and wound re-epithelialization. They are widely used in medical cosmetology such as scar repair. However, the antibacterial effect of recombinant human epidermal growth factor gel preparations is limited, and antibacterial treatment must be taken into account in the treatment of burn patients. At present, there are many reports on the treatment of burn wounds with recombinant human epidermal growth factor combined with antibacterial drugs, such as combined with sulfadiazine zinc and combined with Yinhua Jiedusan. In addition, different research designs are different. Nanosilver dressings are used as controls to observe the therapeutic effects of combined recombinant human epidermal growth factor gel. Sulfadiazine silver is used as a control to analyze the therapeutic effects of recombinant human epidermal growth factor + nanosilver. This study selected the recombinant human epidermal growth factor gel preparation alone as the control to reflect the therapeutic effects of the drug alone and in combination with antimicrobial drugs.

The study found that nanosilver dressing combined with recombinant human epidermal growth factor can significantly shorten the wound healing time and enhance the aesthetic appearance after burns. This study found that nanosilver dressing combined with recombinant human epidermal growth factor gel treatment can significantly reduce the pain of burn patients' wounds, which may be related to the anti-inflammatory effect of nanosilver dressings and the repair of wounds by recombinant human epidermal growth factor gel, which can synergistically reduce pain. The results of this study showed that compared with the use of recombinant human epidermal growth factor gel preparations alone, the wound scab dissolution rate of nanosilver dressing combined with recombinant human epidermal growth factor gel in the treatment of burns was significantly improved at 1 week and 2 weeks of treatment, and the complete scab dissolution time and wound healing time were significantly shortened, which is related to the antibacterial effect of nanosilver and the effect of epidermal growth factor on cell proliferation, division, granulation tissue growth, and wound re-epithelialization. Among them, the possible mechanism of action of nanosilver is: silver particles form silver ions after meeting water, which has a bactericidal effect, and silver particles can be adsorbed on the surface of pathogenic microorganisms, causing microorganisms to sink, and at the same time combine with specific protein groups in pathogens, eventually causing pathogen death; nanosilver can also directly bind to bacterial DNA, affecting cell structure and causing cell death. It can be seen that nanosilver dressing combined with recombinant human epidermal growth factor treatment can not only meet the basic anti-infection of burns, but also promote wound repair and accelerate wound healing. Studies have found that

nanosilver can also promote recombinant human epidermal growth factor to better play the role of repairing wounds, accelerate wound epithelial regeneration and granulation tissue formation, and thus shorten the healing time. At the same time, this study found that in patients with positive bacterial culture, the number of detected bacterial strains was more than the number of patients, indicating that patients with deep second-degree burn wound infection have multiple bacterial colonizations, among which *Pseudomonas aeruginosa* is the most, followed by *Staphylococcus aureus*, providing a reference for the clinical use of antimicrobial drugs.

AGEs and RAGE are related to the degradation of extracellular matrix and play an important role in the degradation of collagen in wounds. The results of this study showed that the expression levels of AGEs and RAGE in the wounds of the observation group after 2 weeks of treatment were significantly lower than those in the control group, suggesting that the nanosilver dressing combined with epidermal growth factor gel preparation may inhibit the expression of AGEs and RAGE in wound tissue to control the degradation of collagen in the wound, avoid the loss of collagen in the wound, and promote wound healing. In terms of safety, this study found that only one patient in the control group had a burning sensation, but it disappeared after 30 minutes, suggesting that nanosilver dressing combined with recombinant human epidermal growth factor is safer for the treatment of burn patients.

Monitoring the expression levels of AGEs and RAGE can reflect the wound healing effect of patients with second-degree burns. The prognosis of the wound is closely related to the expression levels of AGEs, RAGE, and scab abrasion, nanosilver dressings, and mussel mucin spray are used together in the treatment of second-degree burn wounds. Crust abrasion can grasp the level of necrotic scab removal, can achieve "relatively precise" removal of necrotic tissue, maximize the protection of wound ecological tissue and retain normal tissue, and can play a positive role in promoting the healing process of burn wounds; at the same time, nanosilver dressings have good antibacterial properties and high safety, and mussel mucin has anti-inflammatory and antioxidant activity and the characteristics of blocking nerve endings, which can effectively relieve the burning, stinging, and itching of sensitive skin and effectively promote wound healing.

At present, eschar abrasion has been widely used in clinical treatment, but the clinical application research on the combined use of eschar abrasion, nanosilver dressings, and mussel mucin spray in the treatment of second-degree burn wounds is extremely limited. We believe that eschar abrasion, nanosilver dressings, and mussel mucin sprays are used in the treatment of second-degree burn wounds. Eschar abrasion can grasp the level of necrotic scab removal, can achieve "relatively precise" removal of necrotic tissue, and maximize the protection of wound ecological tissue and the preservation of normal tissue, which can play a positive role in promoting the healing process of burn wounds; at the same time, combined with nanosilver dressings and mussel mucin sprays, nanosilver dress-

ings have good antibacterial properties and high safety, and mussel mucin has anti-inflammatory and antioxidant activity and the characteristics of blocking nerve endings, which can effectively relieve the burning, stinging, and itching of sensitive skin and effectively promote wound healing.

In summary, nanosilver dressing combined with epidermal growth factor gel preparation has the characteristics of high scab dissolution rate, short complete scab dissolution time and wound healing time, high bacterial clearance rate and high safety in the treatment of deep second-degree burn wounds. Its wound healing promoting mechanism may be related to the down-regulation of AGEs and RAGE expression.

The study in this paper is limited due to the small sample size, and it is a study conducted in a single hospital and region. In future, the study population will be expanded and conducted across regions, which will bring more accurate conclusions.

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Ethical Statement

The authors are accountable for all aspects of the work and ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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