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Original Article

Effects of silver foam combined with Dermlin wound healing dressing on inflammation and quality of life in patients with diabetic lower limb ulcers

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Abstract: Objective: To investigate the effects of silver foam combined with Dermlin wound healing dressing on concentrations of inflammatory factors of wound surface and quality of life of the patients with diabetic lower limb ulcers. Methods: A total of 60 patients with diabetic lower limb ulcers admitted to the First Affiliated Hospital of Anhui Medical University during January 2020 and December 2020 were retrospectively enrolled in this study. According to the different treatments, they were divided into a control group (30 cases treated with Dermlin wound healing dressing only), and a research group (30 cases treated with silver foam combined with Dermlin dressing). The clinical efficacy, wound healing status, pain intensity (visual analog scale (VAS) scores), concentrations of inflammatory factor (high-sensitivity C-reactive protein (hsCRP), leukocyte interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), procalcitonin (PCT)), angiogenesis factors levels (basic fibroblast growth factor (BFGF), vascular endothelial growth factor (VEGF)), oxidative stress reaction indexes (advanced protein oxidation products (AOPP), malondialdehyde (MDA) and superoxide dismutase (SOD)) and quality of life (SF-36 scale) were compared between two groups. The bacterial removal rate was calculated based on the results of bacterial culture before and after treatment. The central granulated tissue was collected after the granulation tissue coverage rate was calculated. Results: The research group had significantly higher overall response rate (96.67% vs 73.33%), shorter wound healing time and higher wound healing rate than the control group (all $P<0.05$). The VAS scores were decreased in both Groups 1, 3 and 7 d after treatment as compared with those before treatment, and the VAS scores were significantly lower in the research group than in the control group during the same period (all $P<0.05$). After treatment, the concentrations of hsCRP, IL-6, TNF-α, PCT, AOPP and MDA were decreased in both groups, while the levels of bFGF, VEGF, l TGF-β1, SOD and SF-36 scores were increased significantly (all $P<0.05$). The above-mentioned indicators of the research group improved significantly compared with those of the control group (all $P<0.05$). The bacterial removal rate and granulation tissue coverage rate of the research group were significantly higher than those of the control group (both $P<0.05$). Conclusion: The treatment of diabetic lower limb ulcers with silver foam combined with Dermlin dressing can effectively promote wound healing, reduce pain intensity, and improve quality of life in patients with diabetic lower limb ulcers. Such effects may be attributed to lower levels of inflammatory factor levels, regulation of oxidative stress, and improvement of angiogenesis.

Keywords: Silver foam, Dermlin wound healing dressing, diabetic lower limb ulcers, wound surface, inflammatory factors, quality of life

Introduction

Diabetic lower limb ulcers are one of the most prevalent complications of diabetes, which is defined as a lower limb ulceration associated with neuropathy and/or peripheral arterial disease of the lower limb in a patient with diabetes [1]. The ineffective and late management of diabetic lower limb ulcers can lead to enlargement of ulcers that can affect lower limb function and even lower limb amputation, which severely influences patients' life quality [2]. At present, in clinical practice, infection control, wound cleaning, and control of blood sugar level show promising results as the main ways to manage diabetic lower limb ulcers; however,

high hospitalization rate and high levels of antibacterial drug use result in drug-resistant bacterial infections, and unsatisfied wound healing [3, 4]. Therefore, the selection of reasonable and effective antibacterial dressings is of great significance to promote wound healing in patients with diabetic lower limb ulcers. Dermlin dressings, which are commonly used, can effectively stop bleeding, create a good healing environment, but Dermlin dressing alone has limited efficacy with a long wound healing time [5]. In recent years, silver foam dressings have been gradually applied to a variety of wound healing treatment, showing remarkable effects on promoting wound healing and reducing patients' pain [6, 7]. However, there are few reports of the combination of these two in patients with diabetic lower limb ulcers. In view of this, the aim of this study was to investigate the effects of silver foam combined with Dermlin wound healing dressing on inflamation of the diabetic lower limb ulcers, and to explore its possible mechanisms.

Materials and methods

General data

A total of 60 patients with diabetic lower limb ulcers admitted to the First Affiliated Hospital of Anhui Medical University during January 2020 and December 2020 were enrolled in this retrospective research. According to the different treatments, they were divided into a control group (30 cases treated with Dermlin wound healing dressing), and a research group (30 cases treated with silver foam combined with Dermlin dressing). This study had been approved by the Ethics Committee of the First Affiliated Hospital of Anhui Medical University.

Inclusion criteria: (1) Patients who met the diagnostic criteria for diabetic lower limb ulcers [8]. (2) Patients with an age between 18 and 70 years old. (3) Patients in Wagner grades 2 and 3 [9]. (4) Patients with complete clinical data.

Exclusion criteria: (1) Patients who suffered from allergies. (2) Patients in lactation or in pregnancy. (3) Patients with lower limb ulcers resulted from other causes. (4) Patients with limb necrosis that need to undergo amputation. (5) Patients who had taken immunosuppressive drugs and received glucocorticoid therapy recently. (6) Patients with poor compliance. (7) Patients with severe heart, kidney and liver failure.

Methods

After admission, patients in both groups were given oral metformin (H20090050, Beijing Taiyang Pharmaceutical Co., Ltd., China), 0.5 g/time, 3 times/d and oral acarbose (H20213-662, Liaoning Xinshanyuan Pharmaceutical Co., Ltd., China), 50 mg/time, 3 times/d, to control blood sugar levels. At the same time, the wound necrosis tissues were removed. Antibacterial treatments with appropriate antibiotics were carried out based on bacterial culture results. According to the outcome from susceptibility testing for antimicrobials, cefoperazone sodium + sulbactam sodium (3 g) was added to 0.9% sodium chloride injection (10 mL). An intravenous infusion was given once every 12 h, twice a day. Or levofloxacin (750 mg) was added to 0.9% sodium chloride injection (250 mL). An intravenous infusion was given once a day. Patients in the control group were treated with Dermlin dressings. Patients in the research group received silver foam combined with Dermlin dressing. The dressings were changed once a day until the wound healed.

Outcome measures

Clinical efficacy: The clinical efficacy was assessed 7 d after treatment. Markedly effective: clinical symptoms were significantly alleviated or disappeared, and the area of the wound was reduced by 70%-100%. Effective: alleviated clinical symptoms and significantly reduced secretion with the area of the wound shrinking by 50%-70%. Failure to reach the above criteria meant ineffective. Overall response rate = markedly effective rate + effective rate.

Wound healing status: The time and rate of wound healing were recorded.

Pain intensity: The pain intensity was evaluated with visual analogue scale (VAS), which scaled with scores from 0-10, in both groups 1, 3 and 7 d after treatment [10]. The higher scores indicated the severer pain.

Concentrations of inflammatory factor: Fasting vein blood (5 mL) were extracted from patients

Table 1. Comparison of general data (n/$\bar{x}$±sd)

Group	Control group (n=30)	Research group (n=30)	χ^2/t	P
Gender			0.272	0.602
Male	18	16		
Female	12	14		
Age (years)	52.4±4.2	52.7±4.4	0.270	0.788
Course of diabetes (years)	7.36±1.43	7.59±1.51	0.606	0.547
Area of ulcers (cm^2)	15.47±2.47	15.62±2.72	0.224	0.824
Wagner grade (II/III)	15/15	13/17	0.268	0.605

Note: χ^2, data from chi-square statistic; t, data from t-test.

in two groups in the early morning 1 d before treatment and 7 d after treatment, respectively. After centrifugation, high-sensitivity C-reactive protein (hsCRP, YT80045), leukocyte interleukin-6 (IL-6, SEKH-0013), tumor necrosis factor-α (TNF-α, 70-EK182-96), and procalcitonin (PCT, FNab09957) levels were detected with ELISA (EK-Bioscience, Shanghai, China).

Angiogenesis factors levels: ELISA (Jiangxi Aboin Biotechnology Co., Ltd., China) was used to detect basic fibroblast growth factor (BFGF, IB-E10044), vascular endothelial growth factor (VEGF, 50391-M08H) and transforming growth factor-β1 (TGF-β1, HAS-52118) levels 1 d before treatment and 7 d after treatment, respectively.

Oxidative stress reaction indexes: The levels of advanced protein oxidation products (AOPP, HAS-52118, Shanghai Enzyme Linked Biotechnology Co., Ltd.), malondialdehyde (MDA, CS-6142, Shanghai Chuntest Biotechnology Co., Ltd.) and superoxide dismutase (SOD, S10116, Shanghai Yuanye Bio-Technology Co., Ltd.) were detected by spectrophotometer, thiobarbituric acid and Xanthine oxidase assay, respectively, 1 d before treatment and 7 d after treatment.

Patients' quality of life: The patients' quality of life in two groups was assessed using the SF-36 scale before treatment and 3 months after treatment, respectively [11]. The SF-36 scale involves 8 domains, including physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health, with a total score of 100 for each. The higher the scores they are, the better quality of life the patients have.

Bacterial removal rate and granulation tissue coverage rate: The wound secretion was extracted for culture at Day 7 after treatment. Bacterial removal rate = (number of bacteria before debridement-number of bacteria 7 d after treatment)/number of bacteria before debridement *100%. The gridmethod was adopted for granulation tissue coverage rate. Granulation tissue coverage rate = area of granulation tissue coverage/area of wound *100%.

Statistical analysis

SPSS 23.0 software was adopted for statistical analysis. The Shapiro-Wilk test was used to test the normality of the data, which was expressed as mean ± standard deviation ($\bar{x}$±sd). An independent sample t test was carried out for an inter-group comparison and a paired t test was performed for intra-group comparison. Repeated measurement data were tested by F. The counting data were tested with χ^2, and expressed as percentages. P<0.05 was considered statistically significant for differences.

Results

Comparison of general data

No differences were observed in terms of age, gender, course of diabetes, area of ulcers, Wagner grade between two groups (all P>0.05). See **Table 1**.

Comparison of clinical efficacy

The overall response rate of the research group (96.67%) was significantly higher than that of the control group (73.33%; P<0.05). See **Table 2**.

Comparison of wound healing status

Compared with the control group, the research group had significantly shorter wound healing time and higher wound healing rate (both P<0.05). See **Table 3**.

Table 2. Comparison of clinical efficacy (n, %)

Group	Markedly effective rate	Effective rate	Ineffective rate	Overall response rate
Control group (n=30)	12 (40.00)	10 (33.33)	8 (26.67)	22 (73.33)
Research group (n=30)	16 (53.33)	13 (43.33)	1 (3.33)	29 (96.67)
χ^2				4.706
P				0.030

Note: χ^2, data from chi-square statistic.

Table 3. Comparison of wound healing status ($\bar{x}$±sd, n (%))

Group	Wound healing time (d)	Wound healing rate (%)
Control group (n=30)	60.47±4.25	20 (66.67)
Research group (n=30)	51.06±5.02	28 (93.33)
t	7.836	6.667
P	<0.001	0.0001

Note: t, data from t-test.

Table 4. Comparison of pain intensity (scores, $\bar{x}$±sd)

Group	Before treatment	1 d after treatment	3 d after treatment	7 d after treatment
Control group (n=30)	6.25±1.35	4.98±1.01***	3.85±0.68***	3.02±0.57***
Research group (n=30)	6.33±1.02	3.87±0.76***	2.97±0.82***	2.11±0.63***
t	0.259	4.810	4.525	5.867
P	0.797	<0.001	<0.001	<0.001

Note: compared with before treatment in the same group, ***P<0.001. t, data from t-test.

Table 5. Comparison of inflammatory factor levels ($\bar{x}$±sd)

Group	Control group (n=30)	Research group (n=30)	t	P
hs-CRP (mg/L)				
Before treatment	11.36±1.25	11.13±1.34	0.688	0.495
After treatment	7.25±1.01***	4.36±1.16***	10.292	<0.001
IL-6 (pg/mL)				
Before treatment	128.56±21.36	126.28±22.38	0.386	0.701
After treatment	96.35±15.89***	80.14±11.67***	4.504	<0.001
TNF-α (ng/mL)				
Before treatment	46.67±6.85	46.04±7.06	0.725	0.384
After treatment	32.62±5.24***	24.69±5.48***	5.729	<0.001
PCT (ng/mL)				
Before treatment	4.17±1.18	4.44±1.34	0.828	0.411
After treatment	2.65±0.95***	1.32±0.48***	6.844	<0.001

Note: hsCRP, high-sensitivity C-reactive protein; IL-6, leukocyte interleukin-6; TNF-α, tumor necrosis factor-α; PCT, procalcitonin. t, data from t-test. Compared with before treatment in the same group, ***P<0.001.

Comparison of pain intensity

The VAS scores were decreased 1, 3 and 7 d after treatment in both groups, and the VAS scores were significantly lower in the research group during the same period (all P<0.05). See **Table 4**.

Comparison of concentrations of inflammatory factor

After treatment, the concentrations of serum hs-CRP, IL-6, TNF-α, PCT were decreased in both groups, and the research group had significantly lower levels than the control group (all P< 0.05). See **Table 5** and **Figure 1**.

Comparison of angiogenesis factors levels

After treatment, the serum bFGF, VEGF, TGF-β1 1evels were increased in both groups, and the factors in the research group were significantly higher than those in the control group (all P< 0.05). See **Table 6**.

Comparison of oxidative stress reaction indexes

After treatment, the serum AOPP and MDA levels were decreased significantly in both groups, while the SOD levels were increased significantly (all P<0.05). The improvement of the above indicators in the research group was significantly better than those of the control group (all P< 0.05). See **Table 7**.

Comparison of patients' quality of life

After treatment, the SF-36 scores were increased significantly in both groups, and those

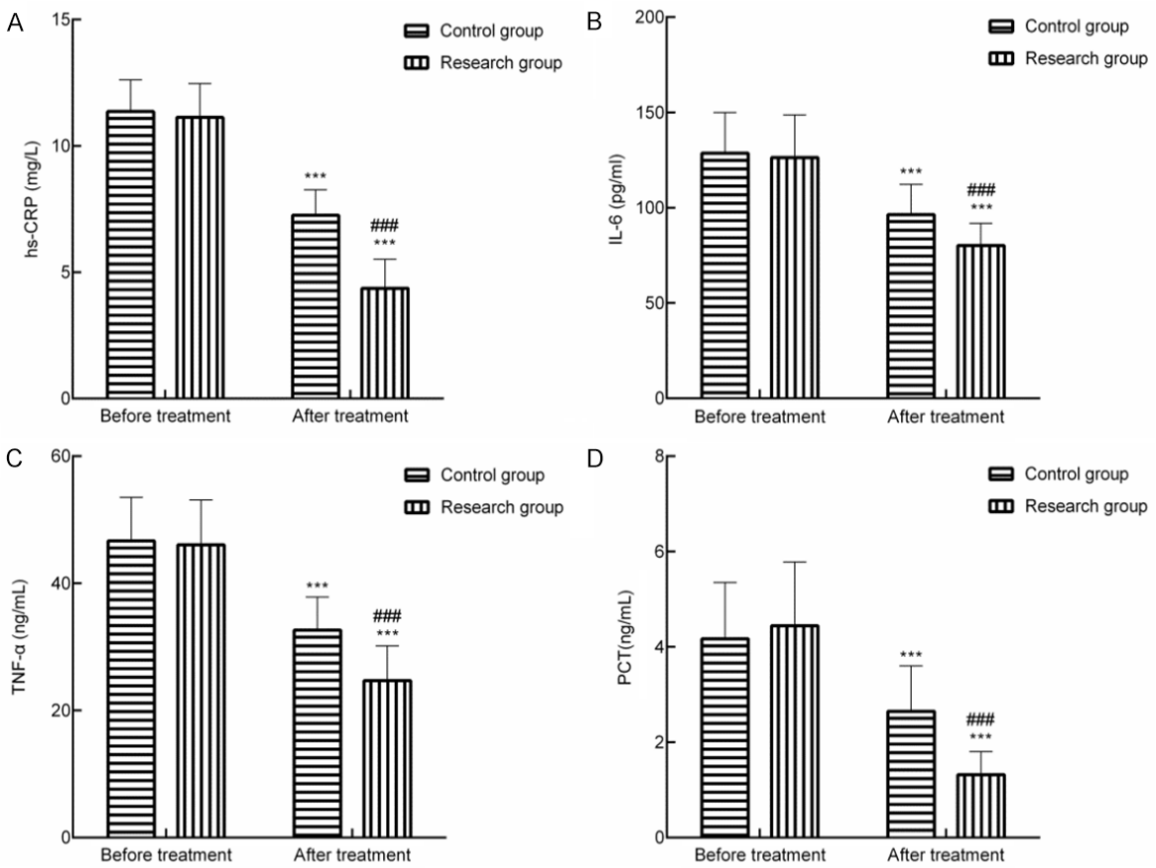

Figure 1. Comparison of inflammatory factor levels. A: hs-CRP; B: IL-6; C: TNF-α; D: PCT. hsCRP, high-sensitivity C-reactive protein; IL-6, leukocyte interleukin-6; TNF-α, tumor necrosis factor-α; PCT, procalcitonin. t-test was used. Compared with before treatment in the same group, ***P<0.001; compared with the control group, ###P<0.001.

Table 6. Comparison of angiogenesis factors ($\bar{x}$±sd, ng/L)

Group	Control group (n=30)	Research group (n=30)	t	P
BFGF (ng/L)				
Before treatment	61.36±5.25	61.13±6.34	0.027	0.979
After treatment	77.25±8.01***	88.36±9.16***	5.001	<0.001
VEGF (pg/mL)				
Before treatment	88.56±10.36	87.28±11.38	0.456	0.765
After treatment	106.35±14.89***	129.14±20.12***	4.987	<0.001
TGF-β1 (ng/L)				
Before treatment	152.37±18.25	153.48±19.17	0.230	0.819
After treatment	201.52±25.24***	248.69±35.48***	5.934	<0.001

Note: bFGF, basic fibroblast growth factor; VEGF, vascular endothelial growth factor; TGF-β, transforming growth factor-β. t, data from t-test. Compared with before treatment in the same group, ***P<0.001.

in the research group was significantly higher than those in the control group (all P<0.05). See **Table 8**.

Comparison of bacterial removal rate and granulation tissue coverage rate

The bacterial removal rate and granulation tissue coverage rate of the research group were significantly higher than those of the control group (both P<0.05). See **Table 9**.

Discussion

In recent years, the incidence of diabetic lower limb ulcers in China has been gradually increased, causing serious negative effects on patients' work and life [12]. The causes of diabetic lower limb ulcers are com-

Table 7. Comparison of oxidative stress reaction ($\bar{x}$±sd)

Group	Control group (n=30)	Research group (n=30)	t	P
AOPP (μmol/L)				
Before treatment	72.72±5.44	72.24±6.15	0.320	0.750
After treatment	60.48±5.12***	48.35±4.47***	9.775	<0.001
MDA (μmol/L)				
Before treatment	28.15±2.01	27.78±2.33	0.655	0.515
After treatment	20.26±1.89***	15.34±1.37***	11.544	<0.001
SOD (IU/L)				
Before treatment	16.25±3.15	16.37±3.21	0.146	0.884
After treatment	24.18±3.34***	29.81±3.41***	6.640	<0.001

Note: AOPP, advanced oxidation protein products; MDA, malondialdehyde; SOD, superoxide dismutase. t, data from t-test. Compared with before treatment in the same group, ***P<0.001.

Table 8. Comparison of patients' quality of life ($\bar{x}$±sd, scores)

Group	Control group (n=30)	Research group (n=30)	t	P
Physical functioning				
Before treatment	65.36±5.25	65.13±5.34	0.168	0.867
After treatment	77.25±7.01***	84.36±6.16***	4.173	<0.001
Bodily pain				
Before treatment	58.56±5.36	58.28±5.38	0.202	0.841
After treatment	76.35±6.89***	85.14±7.67***	4.670	<0.001
Role emotional				
Before treatment	66.67±5.85	66.04±5.06	0.446	0.657
After treatment	73.62±6.24***	84.69±7.48***	6.225	<0.001
Role physical				
Before treatment	64.17±5.18	64.44±5.34	0.817	0.432
After treatment	80.65±6.95***	87.32±7.48***	6.513	<0.001
Mental health				
Before treatment	68.36±5.05	68.13±5.18	0.692	0.487
After treatment	77.25±6.21***	84.36±7.36***	7.385	<0.001
Social functioning				
Before treatment	68.34±5.92	68.11±5.76	0.428	0.682
After treatment	77.25±6.55***	85.14±7.67***	9.504	<0.001
Vitality				
Before treatment	68.24±5.50	68.49±5.19	0.638	0.428
After treatment	78.32±6.18***	85.98±6.33***	5.837	<0.001
General health				
Before treatment	67.38±5.69	67.52±6.77	0.087	0.931
After treatment	77.95±6.11***	86.25±6.92***	8.254	<0.001

Note: t, data from t-test. Compared with before treatment in the same group, ***P<0.001.

plex, which are closely related to high blood sugar status, and metabolic disorders. Tissue hypoxia and ischemia result in lower limb infection, trauma, and the formation of granulated tissue, leading to ulcers under the influence of some factors [13]. At the early stage of diabetic lower limb ulcers, wound cleaning and control of blood sugar level can protect wound surface and reduce the risk of amputation. It is reported that different antibacterial dressings have different effects on promoting wound healing of diabetic lower limb ulcers [14]. Wet dressings can create a moist environment for the wound and promote wound healing. Chitosan based dressings have characteristics of biodegradability, biocompatibility, hemorrhage and wound healing promoting. Nano-silver antibacterial dressings can also prevent infection and promote wound healing.

In this study, the combined use of silver foam and Dermlin wound healing dressing was applied in patients with diabetic lower limb ulcers. The results revealed that the research group had better overall response rate, wound healing status, bacterial removal conditions, VAS scores, and SF-36 scores than the control group, which was consistent with the findings from Li et al. [15]. It was suggested that the combined method had effects on promoting wound healing, reducing pain and improving patients' quality of life. It maybe That Dermlin dressings can effectively absorb blood and seepage fluid with nano-scale micropores, to stop bleeding rapidly, which is not only conducive to wound healing, but also reduces the risk of wound infection [16]. In addition, collagen fibrin secretion and synthesis can be stimu-

Table 9. Comparison of bacterial removal rate and granulation tissue coverage rate ($\bar{x}$±sd, %)

Group	Bacterial removal rate	Granulation tissue coverage rate
Control group (n=30)	80.11±7.14	83.97±5.09
Research group (n=30)	89.12±8.02	92.36±5.37
t	4.596	6.211
P	<0.001	<0.001

Note: t, data from t-test.

lated, inducing epithelial cell proliferation and differentiation, thus shortening the wound healing time. As heavy metal ions, silver ions destroy cell membranes, increase cell permeability, and play an antibacterial role [17]. Silver foam dressings continuously release silver ions, denaturing bacterial proteins and having broad-spectrum activities [18]. At the same time, silver foam dressings can be combined with metallothioneins, and calcium-adjusted proteins. Such treatment will influence the metabolism of microelements, increase the local calcium and zinc ions of the wound surface, accelerate the process of epithelialisation, and thus promote wound healing. Moreover, silver foam dressings may work synergistically with metalloproteinase to inhibit activity and reduce inflammatory response of the wound surface, which helps speed up the wound healing [19, 20]. Last but not the least, silver foam dressings maintain the moist environment of the ulcer surface, which won't stick to the wound surface, and is beneficial to reduce patients' pain during dressing changes [21]. When using foam silver dressings, Li et al. found that silver foam dressings effectively reduced patients' pain, which was consistent with the results of this study [22].

Clinically, inflammatory response is closely related to the wound healing of diabetic lower limb ulcers [23]. When a wound infection occurs, it is difficult to heal the wound because pathogen invasion enhances phagocytosis and wound surface releases a large number of hs-CRP, IL-6 and other inflammatory factors, which all enhance the inflammatory response. Typical inflammatory factors, such ashs-CRP, IL-6, TNF-α, and PCT, can mediate the inflammatory response, promote the local infiltration of inflammatory response. Liu et al. believed that the level of inflammatory factors in patients with diabetic lower limb ulcers was significantly higher than that of the healthy people [24]. Invasive angiogenesis is the key to the healing of diabetic lower limb ulcers and the formation of granulated tissues [25]. BFGF, VEGF, and TGF-β1 can reflect the new blood vessels of the wound, which can be formed in the granulated tissue [26]. In a clinical study, Zheng et al. found that there was a significant oxidative stress response in patients with diabetic lower limb ulcers [27]. Oxidative stress is the physiological and pathological basis of diabetic lower limb ulcers, which not only inhibits antioxidant ability, but also aggravates endocrine disorders and delays wound healing. Detecting the concentrations of SOD, MDA, and AOPP can effectively evaluate the antioxidant ability of patients with diabetic lower limb ulcers [27]. Thus, reducing the inflammatory response, regulating oxidative stress response, and promoting angiogenesis help shorten the healing time of diabetic lower limb ulcers, and improve patients' recovery. In this study, the serum inflammatory factors, angiogenesis factors and oxidative stress indexes in the research group were better than those in the control group. It was indicated that the mechanism of the combined treatment to shorten the wound healing time might be related to lowering the level of inflammatory factors, regulating oxidative stress and promoting angiogenesis.

However, there were still some limitations in this study. The results may be biased due to the small sample size and single center investigation. We did not observe the long-term prognosis of patients with diabetic lower limb ulcers that treated by this combined treatment. Besides, this preliminary study with limited number of cases did not set up a separate silver foam dressing group. In future studies for comparison. Thus, multi-center and large-sample studies with more comprehensive study design should be carried out in the future.

In conclusion, the treatment of diabetic lower limb ulcers with silver foam combined with Dermlin dressing can effectively promote wound healing, reduce pain intensity, and improve patients' quality of life. Its mechanism may be related to lowering inflammatory factor levels, regulating oxidative stress, and promoting angiogenesis.

Disclosure of conflict of interest

None.

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