Int J Clin Exp Med 2020;13(3):1414-1422
www.ijcem.com /ISSN:1940-5901/IJCEM0104426

Original Article

Wet dressings with oxygen-irrigation improves chronic wound healing

Zhenzhen Wang[1], Minmin Yu[2]

Departments of [1]Hepatobiliary Hernia Surgery, [2]Ophthalmootorhinolaryngology, The First People's Hospital of Wenling, Wenling, Zhejiang Province, China

Received November 4, 2019; Accepted December 13, 2019; Epub March 15, 2020; Published March 30, 2020

Abstract: Objective: To study the advantages and benefits of oxygen-irrigated wound negative pressure in the treatment of chronic wounds. Methods: A total of 76 patients with chronic wounds were enrolled and divided into control and observation groups. The patients in the control group were treated with wet dressings while the patients in the observation group were treated with oxygen-irrigated wound negative pressure along with wet dressings. The wound healing rate, the healing time, and the Pressure Ulcer Scale for Healing (PUSH) scores were compared between the two groups at different times. Results: The wound healing rate in the observation group was significantly higher than it was the control group ($P<0.05$), and the healing time, total treatment cost, and dressing change frequencies were significantly lower than they were in the control group (all $P<0.05$). The granulation tissue coverage area in the observation group was significantly higher than it was in the control group ($P<0.05$) after the treatment, but the PUSH scores, wound area, wound depth, and pH of the exudation were significantly lower (all $P<0.05$). Conclusions: Oxygen-irrigated wound negative pressure improves the microenvironment in chronic wounds, contributes to the growth of granulation tissue, and improves the wound healing rate.

Keywords: Wet dressings, oxygen-irrigated wound negative pressure, chronic wounds, curative effect

Introduction

Chronic wounds are wounds in which the three stages of normal healing are incomplete due to various factors, and the wounds are in a state of persistent pathological inflammation. Such wounds are difficult to heal even after active interventions and symptomatic treatment. The etiology of chronic wound formation is complex, and includes systemic, local, and environmental factors [1]. Chronic infection and bacterial biofilm formation are important reasons for chronic wound development.

Studies have confirmed that chronic wounds are unable to repair their complete anatomical structure and function in time, resulting in prolonged hospitalization. This may not only cause serious mood swings and reduce the patients' quality of life, but it may also significantly increase the risk of developing cancer [2]. Traditional systemic antibiotics are ineffective in reaching a therapeutic antimicrobial concentration in the wound, and they can increase the risk of endogenous opportunistic infections. Since 1962, when Dr. Winter discovered that polyethylene can accelerate the keratinization rate of pig wounds, the theory of wet healing has been widely studied and used in clinical practice. Research has shown that wet dressings have many incomparable advantages over dry dressings [3]. They not only promote the formation of wound epithelial cells and the growth of granulation tissue, but they also reduce scab and scar formation and provide an ideal environment for wound healing. Negative pressure wound treatment technology is an effective method for treating acute and chronic wounds as well as war injuries. It absorbs the necrotic tissue and exudates from the wound using negative pressure, and it promotes local blood circulation in the wound and eventually accelerates the growth of wound granulation tissue. The negative pressure absorption device can also act as a wound protective film to avoid exposure to infectious agents [4]. However, negative pressure can lead to hypoxia, and whether the hypoxic environment can promote wound healing is controversial. According to one study, the hypoxic environment can increase the risk of anaerobic bacterial infection and further deteriorate the wound healing process [5]. Hence, a new model of aerobic negative pressure therapy for wounds has been developed. Aerobic negative pressure therapy is a new treatment mode which combines negative pressure therapy and continuous oxygen therapy to avoid the negative effects of the hypoxic environment on wound healing.

In recent years, some progress has been made in treating chronic wounds with wet dressings in combination with oxygen-irrigated wound negative pressure [6]. However, there is still a lack of sufficient evidence outlining this method's benefits compared to traditional wet dressings. Hence, in this study we have evaluated the advantages of oxygen-irrigated wound negative pressure in combination with wet dressings compared to a standalone wet dressings in treating chronic wounds.

Material and methods

General data

Seventy-six patients who came to our hospital with chronic wounds from October 2016 to February 2019 were enrolled as the study subjects. Inclusion criteria: 1) the patients met the diagnostic and classification criteria for chronic wounds [7]; 2) were between 18 and 80 years old; 3) met the indications of oxygen-irrigated wound negative pressure and wet dressings; 4) had no serious cardiovascular and cerebrovascular, liver, kidney, lung or any other substantive organ tissue diseases; 5) volunteered to participate in the study, and signed the informed consent form. Exclusion criteria: 1) patients with untreated osteomyelitis, dry gangrene, precancerous lesions or wound carcinogenesis; 2) patients with systemic infections and on active antibiotic treatment; 3) patients with active hemorrhages or obvious nerve exposure in the wounds; 4) patients with a history of poor compliance; 5) patients suffering from malnutrition, malignant tumors, or other diseases affecting wound healing. The patients were randomly divided equally into a control group and an experimental group (both n=38). There were 23 males and 15 females in the control group, aged 29-77 years, with a mean age of 61.93±6.86 years. The wound types in this group included 16 postoperative incision cases, 11 IV-degree pressure sore cases, 9 trauma cases, and 2 other cases. There were 22 males and 16 females in the experimental group, aged 32 to 79 years, with a mean age of 61.74±6.93 years. The wound types in this group included 16 incision cases, 11 IV-degree pressure sore cases, 9 trauma cases, and 2 other cases. There were no significant differences between the two groups in terms of gender, age, or wound type. This study was approved by the Ethics Committee of The First People's Hospital of Wenling.

Experimental methods

The patients in the control group were only treated with wet dressings. The patients in the experimental group were treated with wet dressings and with oxygen-irrigated negative pressure using the following process. First, the chronic wound was thoroughly cleaned and debrided. Then, the depth and area of the wound were measured. An appropriate wet dressing was selected to cover the wound. Ladder connection pipes, drainage pipes, oxygen irrigated pipes, negative pressure suction pipes, and other pipes were detained, and the wound edge and pipeline were closed with a transparent film dressing. The transparent dressing extended 2 cm from the wound's edges. After the wound treatment was completed, A ZN50 Intelligent Trauma Negative Pressure Comprehensive Treatment Instrument (Shandong Chuangkang Biological Technology Co., Ltd) was used and applied on the affected area for negative pressure suction. The negative pressure device and the drainage pipe were connected to the two ends of the three-way pipe, respectively. The negative pressure treatment parameters were as follows: negative pressure minus 120-130 mmHg; intermittent negative pressure suction mode for 5 min/2 min interval; 24 h/d; procedure lasting 14 days; the dressing and pipeline replacement was done every 3 days. At the same time, oxygen therapy on the wound healing apparatus was given on this basis: oxygen flow rate (3 L/min), temperature (27°C), humidity (65.0%), and 24 hours' continuous oxygen treatment for 14 days. Typical cases are shown in **Figure 1**.

After the treatment, the patients were followed up monthly in the outpatient department for 3 months. The non-healing patients received a

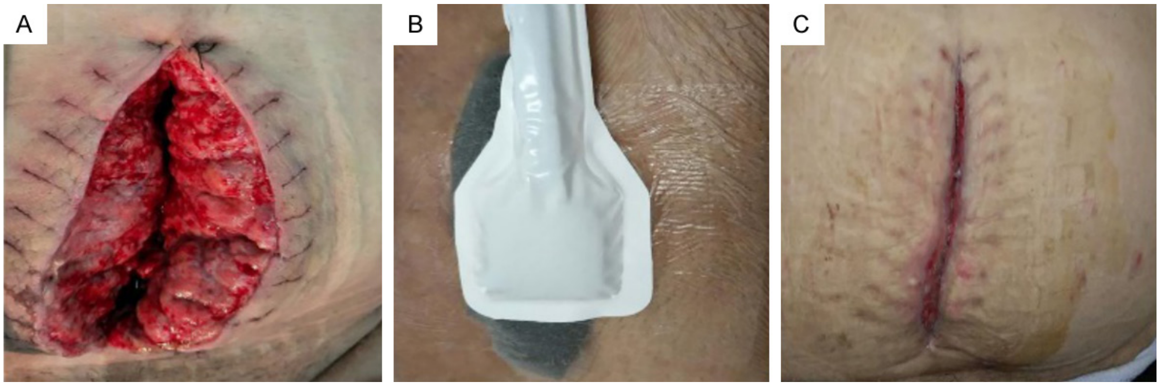

Figure 1. The negative pressure treatment of oxygen-irrigated wounds. A. Chronic wounds after cesarean section before treatment; B. During the negative pressure treatment after the cesarean section; C. Negative pressure treatment after the cesarean section, 1 month later.

Table 1. Comparison of the baseline data

Group	Control group (n=38)	Experimental group (n=38)	P
Wound temperature (°C)	31.93±0.56	32.02±0.59	>0.05
Duration time (weeks)	11.41±1.40	11.63±1.51	>0.05
Bacterial positive rate (%)	27 (71.05)	29 (76.31)	>0.05
Fat liquefaction	15 (39.48)	17 (44.74)	>0.05
Diabetes mellitus	20 (52.63)	22 (57.89)	>0.05
Obesity	26 (68.42)	25 (65.79)	>0.05
Hypertension	17 (44.74)	18 (47.37)	>0.05
Previous treatment duration (days)	9.47±0.66	9.53±0.70	>0.05

Table 2. Comparison of the wound healing rate, healing time, total treatment cost, and dressing change frequency

Group	Control group (n=38)	Experimental group (n=38)	t/χ^2	P
Wound healing rate (n, %)	23 (60.53)	34 (89.47)	χ^2=8.491	0.003
Wound healing time (days)	39.64±5.82	26.71±4.06	t=11.232	0.000
Total treatment cost (RMB)	8367±1538	6013±1065	t=9.647	0.000
Dressing change frequency	17.98±5.60	9.74±3.38	t=7.765	0.000

re-treatment, and their healing time was not included in the evaluation.

Experimental indicators and evaluation criteria

1) The baseline data, such as wound temperature, duration time, bacterial positive rate, fat liquefaction, diabetes mellitus, obesity, hypertension, and previous treatment duration were compared between the two groups. 2) The wound healing rate, healing time, total treatment cost, and dressing replacement frequencies of the two groups were compared after 3 months of treatment. The dressing replacement criteria were as follows: bleeding, exudation, pressing pain, or other signs of infection, and the integrity of the dressing being damaged, wet or loose. 3) We recorded the healing scores, wound areas, wound depths, pH of the exudate and granulation tissue coverage in the two groups before and after the treatment for 3, 7, 10, and 14 days. The Pressure Ulcer Scale for Healing (PUSH) was used to assess the patients' wound healing scores, including the wound surface areas, 24-hour wound exudate volumes, and tissue types. The higher the score calculated by PUSH, the worse the wound healing. Granulation tissue coverage = granulation tissue area/wound area * 100.0%. The wound healing was considered complete when the entire area was covered with wound epithelium, and no oxidative reaction was observed when 3.0% hydrogen peroxide was applied to the wound [8].

Statistical methods

SPSS21.0 software was used to analyze all the raw data in this study. The data were expressed in the form of $\overline{x}$±sd. Independent sample t tests were used for the comparisons between the two groups, and multiple time points were analyzed using repeated measurement analy-

Table 3. Comparison of the PUSH scores at different time points before and after the treatment ($\overline{x}\pm$sd)

Group	Control group (n=38)	Experimental group (n=38)	t	P
Before treatment	15.23±1.60	14.83±1.56	1.103	0.273
3 d after treatment	11.93±1.40	11.46±1.03	1.667	0.100
7 d after treatment	$10.87\pm1.22^{*,\wedge}$	$8.43\pm1.12^{*,\&,\wedge}$	9.082	0.000
10 d after treatment	$9.53\pm1.02^{*,\wedge,\%}$	$6.29\pm0.86^{*,\&,\wedge,\%}$	14.97	0.000
14 d after treatment	$7.61\pm0.73^{*,\wedge,\%,\#}$	$4.81\pm0.65^{*,\&,\wedge,\%,\#}$	17.659	0.000
F	9.473	15.391		
P	0	0		

Note: Compared with before treatment in the same group, *P<0.05; compared with control group at the same time point, &P<0.05; compared with 3d after the treatment in the same group, ^P<0.05; compared with 7d after the treatment in the same group, %P<0.05; compared with 10d after the treatment in the same group, #P<0.05; PUSH, Pressure Ulcer Scale for Healing.

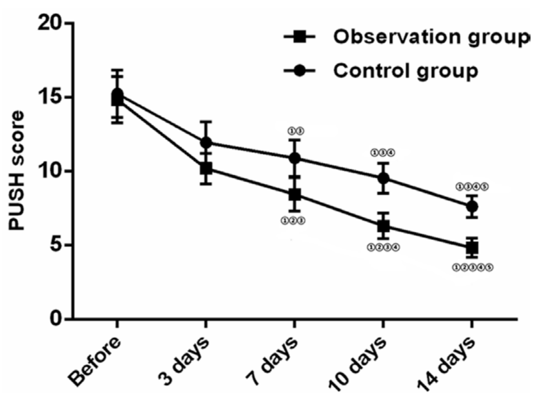

Figure 2. Comparison of the PUSH scores at different time points before and after the treatment. Compared with before treatment in the same group, ①P<0.05; compared with control group at the same time point, ②P<0.05; compared with 3 d after the treatment in the same group, ③P<0.05; compared with 7 d after the treatment in the same group, ④P<0.05; compared with 10 d after the treatment in the same group, ⑤P<0.05; PUSH, Pressure Ulcer Scale for Healing.

ses of variance combined with post hoc Bonferroni tests. The individual counts were expressed using percentages. Chi-square tests were performed between groups to evaluate the differences between the different parameters measured for wound healing. A difference was considered statistically significant when *P*<0.05.

Results

Comparison of the baseline data

The wound temperature, duration time, bacterial positive rate, fat liquefaction, diabetes mellitus, obesity, hypertension, and previous treatment duration baseline data between the two groups showed no significant differences (all P>0.05), as shown in **Table 1**.

Comparison of the wound healing rates, healing times, total treatment costs, and dressing change frequencies

The wound healing rate in the experimental group was significantly higher than it was in the control group (P<0.05). The healing time, total treatment cost, and dressing replacement frequencies in the experimental group were significantly lower than they were in the control group (all P<0.05) (**Table 2**).

Comparison of the PUSH scores at different time points before and after the treatment

There was no significant differences in the PUSH scores between the two groups before and 3 days after the treatment (both P>0.05). However, at 7, 10, and 14 days after the treatment, the experimental group's PUSH scores were significantly lower than those of the control group (all P<0.01). Details are shown in **Table 3** and **Figure 2**.

Comparison of wound areas at different time points before and after the treatment

There was no significant difference in the wound areas between the two groups before and 3 days after the treatment (both P>0.05). However, after 7, 10, and 14 days of treatment, the wound areas in the experimental group were significantly lower than they were in the control group (all P<0.01), as shown in **Table 4** and **Figure 3**.

Comparison of the wound depths at different time points before and after the treatment

There was no significant difference in the wound depths between the two groups before and 3 days after the treatment (both P>0.05). However, at 7, 10, and 14 days after the treatment, the wound depths in the experimental

Table 4. Comparison of the wound areas at different time points before and after the treatment (cm^2, $\overline{x}\pm sd$)

Group	Control group (n=38)	Experimental group (n=38)	t	P
Before treatment	18.04±7.83	18.19±7.90	0.083	0.934
3 d after treatment	13.91±6.52	11.75±4.87	1.636	0.106
7 d after treatment	$10.78\pm6.13^{*,\wedge}$	$6.63\pm3.81^{*,\&,\wedge}$	3.545	0.000
10 d after treatment	$6.92\pm3.26^{*,\wedge,\%}$	$2.86\pm1.83^{*,\&,\wedge,\%}$	6.694	0.000
14 d after treatment	$3.88\pm2.35^{*,\wedge,\%,\#}$	$1.69\pm1.44^{*,\&,\wedge,\%,\#}$	4.898	0.000
F	9.462	14.376		
P	0	0		

Note: Compared with before treatment in the same group, *P<0.05; compared with control group at the same time point, $^{\&}$P<0.05; compared with 3d after the treatment in the same group, $^{\wedge}$P<0.05; compared with 7 d after the treatment in the same group, $^{\%}$P<0.05; compared with 10 d after the treatment in the same group, $^{\#}$P<0.05.

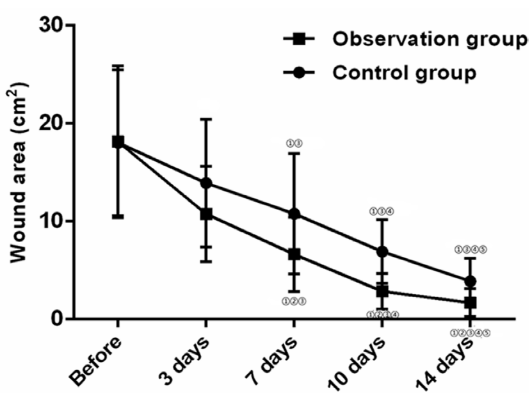

Figure 3. Comparison of wound areas at different time points before and after the treatment. Compared with before treatment in the same group, ①P<0.05; compared with control group at the same time point, ②P<0.05; compared with 3 d after the treatment in the same group, ③P<0.05; compared with 7 d after the treatment in the same group, ④P<0.05; compared with 10 d after the treatment in the same group, ⑤P<0.05.

group were significantly lower than they were in the control group (all P<0.01), as shown in **Table 5** and **Figure 4**.

Comparison of the granulation tissue coverage ratio at different time points before and after the treatment

There was no significant difference in the coverage of the granulation tissue between the two groups at 3 days post treatment (P>0.05). However, on the 7th, 10th, and 14th days post treatment, the granulation tissue coverage in the experimental group was significantly higher than it was in the control group (all P<0.01), as shown in **Table 6** and **Figure 5**.

Comparison of exudate pH at different time points before and after the treatment

There was no significant difference in the exudate pH between the two groups before and at 3 days after the treatment (both P>0.05). On the 7th, 10th, and 14th days after the treatment, however, the pH of the exudate in the experimental group was significantly lower than it was in the control group (all P<0.01), as shown in **Table 7** and **Figure 6**.

Discussion

The quality of wound healing is affected by many factors, including the treatment method, nursing, and self-function, etc. [9]. An accurate assessment of the wound parameters is particularly critical in improving the wound healing rate. For chronic wound treatment, a detailed assessment is needed, including what caused the wound, the initial wound manifestations, the pain, and the previous treatment and diagnosis history. A study has confirmed that traditional systemic antibiotics can increase the risk of endogenous opportunistic infections and have limited therapeutic effects on chronic wounds [10]. Since 1962, the theory of wet healing has drawn increased attention, and wet dressings have become widely used. Many studies have pointed out that the humid environment created by wet dressings not only reduces the chance of infection, but it also has many unique advantages over dry dressings [11-14]. These include increasing the proliferation and migration of the peripheral epidermal cells, improving the oxygen tension, temperature, and humidity of the wound surface, and increasing the granulation tissue growth and angiogenesis. Wet dressings are conducive to wound necrosis tissue and fibrinolysis absorption, and they protect the nerve endings in the wound, thereby reducing pain. At the same time, dressings can provide exogenous nutrients, promote the release of the immune and wound healing factors, and avoid cross-infection with the surrounding bacteria. A wet environment can enhance the local bacteriostatic ability and help the formation and growth of

Table 5. Comparison of wound depths at different time points before and after the treatment (cm, $\bar{x}\pm$sd)

Group	Control group (n=38)	Experimental group (n=38)	t	P
Before treatment	2.11±0.94	2.07±0.99	0.181	0.857
3 d after treatment	1.73±0.80	1.51±0.67	1.129	0.198
7 d after treatment	$1.32\pm0.69^{*,\wedge}$	$0.92\pm0.54^{*,\&,\wedge}$	2.814	0.006
10 d after treatment	$1.03\pm0.61^{*,\wedge,\%}$	$0.65\pm0.43^{*,\&,\wedge,\%}$	3.139	0.002
14 d after treatment	$0.88\pm0.46^{*,\wedge,\%,\#}$	$0.42\pm0.27^{*,\&,\wedge,\%,\#}$	5.316	0.000
F	5.36	10.458		
P	0	0		

Note: Compared with before treatment in the same group, $^{*}P<0.05$; compared with control group at the same time point, $^{\&}P<0.05$; compared with 3 d after the treatment in the same group, $^{\wedge}P<0.05$; compared with 7 d after the treatment in the same group, $^{\%}P<0.05$; compared with 10 d after the treatment in the same group, $^{\#}P<0.05$.

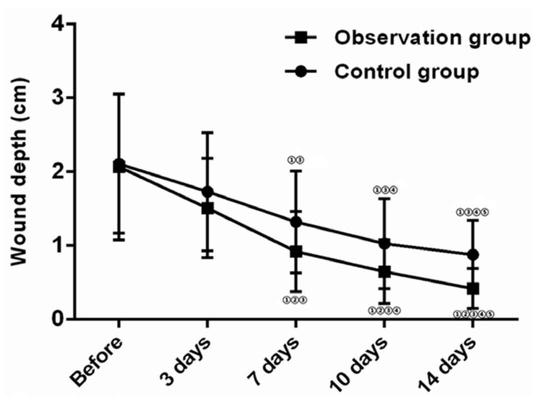

Figure 4. Comparison of the wound depths at different time points before and after the treatment. Compared with before the treatment in the same group, ①P<0.05; compared with the control group at the same time point, ②P<0.05; compared with 3 d after the treatment in the same group, ③P<0.05; compared with 7 d after the treatment in the same group, ④P<0.05; compared with 10 d after the treatment in the same group, ⑤P<0.05.

wound granulation tissue. Studies show that the infection rate in traditional dressings in traumatic wounds is as high as 7.1%, while the rate in wet dressings is only 2.6% [15]. At present, wet dressings have proved to be useful in shortening the wound healing time, while reducing the patients' wound pain and cost burdens for the treatment of pressure ulcers, lower limb venous ulcer wounds, diabetic foot ulcers, radiation-induced skin injuries, and post-operative refractory wounds.

Negative pressure technology is a new method of wound treatment that has been utilized in recent years. It mainly uses a controllable negative pressure absorption device to form a closed vacuum environment between the connecting tube and the wound. It covers the wound with a transparent membrane, removes contact between the wound and air and reduces infection, so as to accelerate wound healing [16]. Studies have confirmed that negative pressure technology has many therapeutic advantages, including maintaining the active drainage and ensuring the timely drainage of wound exudation and necrotic tissue, while reducing the local tissue edema [17]. Negative pressure can increase the blood perfusion of the local tissue, ensure the moistness of the tissue around the wound, and accelerate the growth of granulation tissue and epithelial tissue repair. At the same time, the negative pressure maintained in a closed environment greatly reduces the risk of bacterial infection. Negative pressure devices also reduce the requirement of frequent medical care, reduces the waste of resources, and reduces the pain when changing dressings. However, whether the hypoxic environment created by the negative pressure technology can promote wound healing is controversial. A hypoxic environment can increase the risk of anaerobic bacterial infection and may worsen the wound healing environment. Therefore, a new model of aerobic negative pressure treatment has been developed for chronic wounds. Studies have shown that the partial oxygen pressure in the wound tissue is closely related to the quality of wound healing [18]. Although hyperbaric oxygen therapy can significantly improve the partial oxygen pressure in the wound tissue, it can also lead to the excessive release of reactive oxygen species (ROS), resulting in severe lipid peroxidation and ultimately an increase in wound tissue damage. Therefore, appropriate partial oxygen pressure is essential to promote wound healing. Ropaz et al. succeeded in treating anaerobic bacteria infected wounds with negative pressure in combination with local oxygen therapy for the first time in 2011 [19]. Hence, the combination of the two methods has been widely used since then in the treat-

Table 6. Comparison of the granulation tissue coverage ratio at different time points before and after the treatment (%, $\overline{x}$±sd)

Group	Control group (n=38)	Experimental group (n=38)	t	P
3 d after treatment	11.76±2.17	12.72±2.60	1.747	0.084
7 d after treatment	$15.93 \pm 4.30^{\wedge}$	$22.48 \pm 5.13^{\wedge,\&}$	6.032	0.000
10 d after treatment	$28.92 \pm 7.10^{\wedge,\%}$	$37.81 \pm 6.93^{\wedge,\&,\%}$	5.524	0.000
14 d after treatment	$42.74 \pm 8.42^{\wedge,\%,\#}$	$58.49 \pm 9.68^{\wedge,\&,\%,\#}$	7.568	0.000
F	6.054	9.649		
p	0	0		

Note: Compared with control group at the same time point, $^{\&}$P<0.05; compared with 3 d after the treatment in the same group, $^{\wedge}$P<0.05; compared with 7 d after the treatment in the same group, $^{\%}$P<0.05; compared with 10 d after the treatment in the same group, $^{\#}$P<0.05.

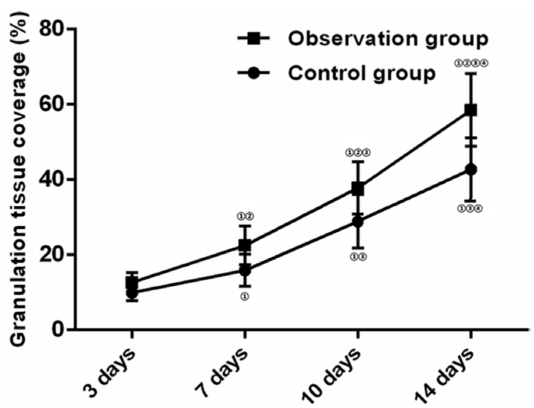

Figure 5. Comparison of the granulation tissue coverage ratio at the different time points before and after the treatment. Compared with 3 d after the treatment in the same group, ①P<0.05; compared with the control group at the same time point, ②P<0.05; compared with 3 d after the treatment in the same group, ③P<0.05; compared with 7 d after the treatment in the same group, ④P<0.05.

ment of wounds. It has been shown in clinical practice that the partial oxygen pressure in the wound tissue can be maintained at about 50-100 mmHg by a continuous infusion of 2-3 L/min of oxygen flow into the wound, thereby, increasing the local vasodilation, arterial partial oxygen pressure, and molecular oxygen permeation [20]. A steady oxygen flow rate improves local oxygen partial pressure and the healing speed of wounds, but it has no oxygen toxicity. K Copeland et al. found that the total effective rate of local oxygen therapy for chronic wounds such as diabetic skin ulcers, postoperative gangrene, bedsore ulcers, skin transplantations, burns and frostbites was 59.4%, and the total amputation rate was only 2.4%, suggesting that local oxygen therapy can improve the healing of chronic wounds [21]. Bsc et al. showed that local oxygen therapy can significantly shorten the healing time of refractory diabetic foot ulcers and lead to their complete recovery [22]. Bradbury et al. also showed that a local negative pressure device could promote the growth of granulation tissue in chronic wounds such as leg ulcers and nervous foot ulcers, relieve wound pain and exudate, and reduce the wound area by 42.64% on average [23]. In this study, we selected the recommended oxygen flow of 3 L/min, a temperature of 27°C, a humidity of 65.0%, with a combination of negative pressure technology and wet dressings to treat chronic wounds. The observations showed that the wound healing rate in the experimental group was 89.47%, significantly higher than the rate in the control group (60.53%). The healing time, total treatment costs, and dressing replacement frequencies in the experimental group were significantly lower than they were in the control group. In addition, the PUSH scores, wound areas, wound depths, granulation tissue coverage rate, and exudate pH are considered to be the parameters of wound healing. The observations showed that the PUSH scores, wound area, wound depth, and exudate pH in the experimental group were significantly lower than they were in the control group at 7, 10, and 14 days after the treatment, while the granulation tissue coverage rate in the experimental group was significantly higher than it was in the control group. In the initial stage of treatment, massive tissue exudation and tissue edema led to the increased diffusion of oxygen molecules [24]. Also, the presence of carrion in the wound can affect oxygen permeation, resulting in a slow healing of the wound area. Therefore, the improvement in the wound healing index is relatively insignificant in the first few days. However, after 7 days of treatment, due to the improvement in the wound exudation drainage and tissue edema, the oxygen diffusion decreases significantly. The oxygen-irrigated negative pressure sealing therapy improves angiogenesis, tissue perfusion improvement, necrotic tissue and exudation drainage, so as to increase

Table 7. Comparison of the exudate pH at different time points before and after the treatment ($\bar{x}$±sd)

Group	Control group (n=38)	Experimental group (n=38)	t	P
Before treatment	8.40±0.32	8.38±0.35	0.26	0.796
3 d after treatment	8.17±0.26	8.04±0.27	1.645	0.104
7 d after treatment	7.95±0.30$^{*,\wedge}$	7.46±0.23$^{*,\&,\wedge}$	7.991	0.000
10 d after treatment	7.72±0.26$^{*,\wedge,\%}$	7.31±0.20$^{*,\&,\wedge,\%}$	7.705	0.000
14 d after treatment	7.50±0.24$^{*,\wedge,\%,\#}$	7.16±0.17$^{*,\&,\wedge,\%,\#}$	7.126	0.000
F	7.828	14.375		
P	0	0		

Note: Compared with before treatment in the same group, *P<0.05; compared with control group at the same time point, $^{\&}$P<0.05; compared with 3 d after the treatment in the same group, $^{\wedge}$P<0.05; compared with 7 d after the treatment in the same group, $^{\%}$P<0.05; compared with 10 d after the treatment in the same group, $^{\#}$P<0.05.

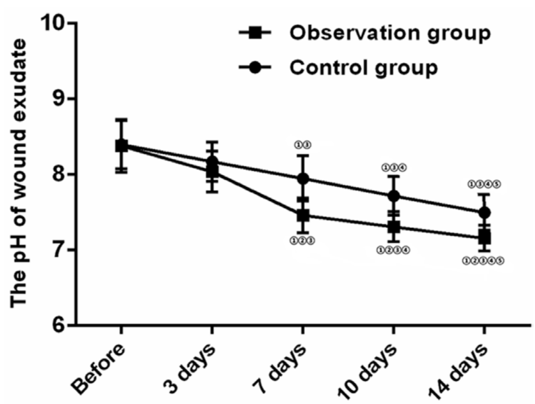

Figure 6. Comparison of the exudate pH levels at the different time points before and after the treatment. Compared with before the treatment in the same group, ①P<0.05; compared with the control group at the same time point, ②P<0.05; compared with 3 d after the treatment in the same group, ③P<0.05; compared with 7 d after the treatment in the same group, ④P<0.05; compared with 10 d after the treatment in the same group, ⑤P<0.05.

the proliferation of granulation tissue around the wound and accelerate wound healing. Therefore, necrotic tissues and carrion should be removed thoroughly before starting oxygen-irrigated negative pressure sealing therapy, thereby increasing oxygen penetration into the wound tissue and promoting granulation tissue growth and wound healing [25].

However, due to the small size of the cohort, the short intervening time, and the lack of long-term follow-up observations, this study's conclusion has some limitations. The observations in this study need to be replicated in a larger sample size and must be followed-up for a longer time in future studies.

In conclusion, wet dressings combined with oxygen-irrigated negative pressure can significantly improve the micro-environment in chronic wounds, promote wound granulation tissue growth, accelerate the wound healing time and rate, and ultimately reduce patients' medical costs, which is worthy of clinical promotion.

Disclosure of conflict of interest

None.

Address correspondence to: Minmin Yu, Department of Ophthalmootorhinolaryngology, The First People's Hospital of Wenling, No. 333 Chuan'an South Road, Chengxi Street, Wenling 317500, Zhejiang Province, China. Tel: +86-13586278757; E-mail: yuminmin5ymm1@163.com

References

[1] Hesketh M, Sahin KB, West ZE and Murray RZ. Macrophage phenotypes regulate scar formation and chronic wound healing. Int J Mol Sci 2017; 18.

[2] Lazaro JL, Izzo V, Meaume S, Davies AH, Lobmann R and Uccioli L. Elevated levels of matrix metalloproteinases and chronic wound healing: an updated review of clinical evidence. J Wound Care 2016; 25: 277-287.

[3] Hiranpattanakul P, Jongjitpissamai T, Aungwerojanawit S and Tachaboonyakiat W. Fabrication of a chitin/chitosan hydrocolloid wound dressing and evaluation of its bioactive properties. Res Chem Intermediates 2018; 44: 1-16.

[4] Masters JPM, Achten J, Cook J, Dritsaki M, Sansom L and Costa ML. Randomised controlled feasibility trial of standard wound management versus negative-pressure wound therapy in the treatment of adult patients having surgical incisions for hip fractures. BMJ Open 2018; 8: e020632.

[5] Stroot PG. Blood oxidative stress (BLOS) is a secondary host defense system responding normally to anaerobic wound infection and inadvertently to dietary ultra-exogenous sulfide formation (USF). Med Hypotheses 2017; 98: 28-34.

[6] Teot L, Boissiere F and Fluieraru S. Novel foam dressing using negative pressure wound thera-

py with instillation to remove thick exudate. Int Wound J 2017; 14: 842-848.
[7] Majchrzak E, Dziewoński M, Nowak M, Kawecki M, Bachorz M and Kowalski P. The design of a system for assisting burn and chronic wound diagnosis 2012.
[8] Rahman N, Rahman H, Haris M and Mahmood R. Wound healing potentials of Thevetia peruviana: antioxidants and inflammatory markers criteria. J Tradit Complement Med 2017; 7: 519-525.
[9] Ueck C, Volksdorf T, Houdek P, Vidal YSS, Sehner S, Ellinger B, Lobmann R, Larena-Avellaneda A, Reinshagen K, Ridderbusch I, Kohrmeyer K, Moll I, Daniels R, Werner P, Merfort I and Brandner JM. Comparison of in-vitro and ex-vivo wound healing assays for the investigation of diabetic wound healing and demonstration of a beneficial effect of a triterpene extract. PLoS One 2017; 12: e0169028.
[10] Hernandez R. The use of systemic antibiotics in the treatment of chronic wounds. Dermatol Ther 2006; 19: 326-337.
[11] Kumar A and Jaiswal M. Design and in vitro investigation of nanocomposite hydrogel based in situ spray dressing for chronic wounds and synthesis of silver nanoparticles using green chemistry. J Appl Polym Sci 2016; 133.
[12] Ivins N, Braumann C, Kirchhoff JB, Waldemar U and Jones NJ. Use of a gelling fibre dressing in complex surgical or chronic wounds: a case series. J Wound Care 2018; 27: 444-454.
[13] Zolss C and Cech JD. Efficacy of a new multifunctional surfactant-based biomaterial dressing with 1% silver sulphadiazine in chronic wounds. Int Wound J 2016; 13: 738-743.
[14] Ricci E and Cutting KF. Evaluating a native collagen matrix dressing in the treatment of chronic wounds of different aetiologies: a case series. J Wound Care 2016; 25: 670-678.
[15] Muensterer OJ and Keijzer R. A simple vacuum dressing reduces the wound infection rate of single-incision pediatric endosurgical appendectomy. JSLS 2011; 15: 147-150.
[16] Blume PA, Walters J, Payne W, Ayala J and Lantis J. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. Diabetes care 2008; 31: 631-636.
[17] Chiang N, Rodda OA, Sleigh J and Vasudevan T. Effects of topical negative pressure therapy on tissue oxygenation and wound healing in vascular foot wounds. J Vasc Surg 2017; 66: 564-571.
[18] Bychkov SF, Gainutdinov II, Chizhik SA and Nemudry AP. Novel oxygen partial pressure relaxation technique for study of oxygen exchange in nonstoichiometric oxides. The model of relaxation kinetics. Solid State Ion 2018; 320: 297-304.
[19] Topaz M, Bisker O, Litmanovitch M and Keren G. Application of regulated oxygen-enriched negative pressure-assisted wound therapy in combating anaerobic infections. J Plast Reconstr Aesthet Surg 2011; 34: 351-358.
[20] Topaz M. Improved wound management by regulated negative pressure-assisted wound therapy and regulated, oxygen- enriched negative pressure-assisted wound therapy through basic science research and clinical assessment. Indian J Plast Surg 2012; 45: 291-301.
[21] Copeland K and Purvis AR. A retrospective chart review of chronic wound patients treated with topical oxygen therapy. Adv Wound Care 2017; 6: 143-152.
[22] Yu J, Lu S, McLaren AM, Perry JA and Cross KM. Topical oxygen therapy results in complete wound healing in diabetic foot ulcers. Wound Repair 2016; 24: 1066-1072.
[23] Bradbury S, Walkley N, Ivins N and Harding K. Clinical evaluation of a novel topical negative pressure device in promoting healing in chronic wounds. Adv Wound Care 2015; 4: 346-357.
[24] Rippon MG, Ousey K and Cutting KF. Wound healing and hyper-hydration: a counterintuitive model. J Wound Care 2016; 25: 68, 70-65.
[25] Wolvos T. The evolution of negative pressure wound therapy: negative pressure wound therapy with instillation. J Wound Care 2015; 24: 15-20.