Received: 13 June 2022 | Revised: 19 July 2022 | Accepted: 19 July 2022

DOI: 10.1111/iwj.13911

ORIGINAL ARTICLE

IWJ WILEY

Clinical efficacy of wet dressing combined with chitosan wound dressing in the treatment of deep second-degree burn wounds: A prospective, randomised, single-blind, positive control clinical trial

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Abstract

To evaluate the efficacy and safety of wet dressing combined with chitosan wound dressing for deep II degree burn wounds, and provide the basis for clinical application. From October 2019 to October 2021, 80 patients with second-degree deep burn treated in the Department of burn and plastic surgery of our hospital were selected as the research objects. Patients were randomly divided into two groups. The control group (40n) was treated with wet compress, and the study group (40n) was treated with wet compress combined with chitosan wound dressing. The wound healing time, wound healing percentage and pain score were used as the effectiveness indexes, and the incidence of adverse events and serious adverse events and the detection rate of bacterial culture of wound exudates were used as the safety indexes. The efficacy and safety of the two groups were compared. The wound healing time of the study group (19.53 $\pm$ 2.74 days) was shorter than that of the control group (24.78 $\pm$ 4.86 days), the difference was significant ($t = 3.571$, $P = 0.015$). The percentage of wound healing at the 14th after treatment in the study group was higher than that in the control group (65.00% versus 37.50%) ($X^2 = 6.054$, $P = 0.014$). There was no significant difference in pain scores between the two groups at each time point. The scar growth was observed 3 months after wound healing. The scar score of the study group (6.00 $\pm$ 0.98) was lower than that of the control group (8.77 $\pm$ 1.19) ($t = 2.571$, $P = 0.031$). The positive rate of wound secretion culture on the 7th and 14th day was statistically significant ($X^2 = 4.528$, $P = 0.033$; $X^2 = 6.646$, $P = 0.010$), and the study group was lower than the control group (29.03% versus 81.82%; 8.11% versus 42.86%). There was no significant difference in treatment cost between the study

group and the control group (1258.7 ± 223.6 versus 1248.9 ± 182.3) ($t = 1.571$, $P = 0.071$). No adverse events or serious adverse events occurred in both groups. Chitosan wound dressing can significantly shorten the time of wound healing and reduce wound pain and wound infection in patients with deep second-degree burns. And it can effectively improve the situation of scar hyperplasia, which is worthy of clinical application.

KEYWORDS

chitosan wound dressing, clinical application, deep second-degree burn, wet dressing, wound healing

Key Messages

- the main purpose of burn treatment is not only to save lives, reduce patients' pain and quickly heal wounds
- this study aims to evaluate the efficacy and safety of wet dressing combined with chitosan wound dressing for deep II degree burn wounds, and provide the basis for clinical application
- the use of et healing combined with chitosan dressing in the treatment of deep second-degree burn can reduce the wound infection rate on the 7th and 14th days, shorten the healing time, and reduce scar hyperplasia 3 months after healing

1 | INTRODUCTION

Due to the destruction of skin barrier function, the immune function of burn patients decreased. The risk of wound bacterial infection is high, and even endanger the life safety of patients in serious cases.[1] Therefore, burn patients should be treated reasonably as soon as possible to promote wound healing and improve skin function. To avoid further deterioration of the disease.[2] At present, debridement and disinfection, external application of drugs or dressings are often used to treat burn wounds in clinic[3,4] Among them, external application of dressing has achieved good clinical effect in reducing wound infection and promoting wound healing. However, the choice of external application materials can directly affect the wound healing effect.

Chitosan is a kind of bioactive polysaccharide with positive charge. The wound dressing prepared from chitosan not only has the functions of natural bacteriostasis, haemostasis and promoting wound healing.[5] And it has good biocompatibility, biodegradability and biological function. It is widely used in the treatment of surgical trauma and burns.[6] In this study, chitosan wound dressing was applied to the treatment of deep second-degree burn wounds. To evaluate the efficacy and safety of wet dressing combined with chitosan wound dressing in the treatment of deep second-degree burns, to provide basis for clinical application. Now it is reported as follows.

2 | PATIENTS AND METHODS

2.1 | Study population

A total of 80 patients with second-deep degree burn admitted to the Burn Plastic Department of our Hospital from October 2019 to October 2021 were selected as the research objects.

Inclusion criteria: ① 18 to 60 years old; ② patients were admitted to hospital within 24 h after flame or hydrothermal burns without any treatment before admission; ③ The wound was asymptomatic, and the depth of burn was deep II degrees. Burn area the total burn area is 5% to 10% of the total body surface area; ④ the patient was not allergic constitution, no immune disease and no nutritional metabolic diseases; ⑤ patients or clients agreed to participate in this clinical trial, and could understand and sign the informed consent; ⑥ good compliance, willingness and ability to follow-up observation as required.

Exclusion criteria: ① patients with allergic history of multiple drugs or recent allergic diseases; ② those allergic to seafood such as shrimp and crab; ③ pregnant women and lactating women; ④ patients with mental disorders and those without self-awareness and accurate expression; ⑤ patients who participated in clinical trials of other drugs or instruments within 3 months before admission.

2.2 | Study design

The study was a randomised, open, parallel controlled clinical trial. The study was approved by the Medical Ethics Committee of Our Hospital. The random distribution table was generated according to the method of randomised block. For the subjects who signed the informed consent and met the criteria, the random distribution envelope was opened according to the order before and after enrolment. After obtaining the random results, the researcher signed the name and time of the reader in the random distribution letter, and treated the subjects according to the distribution group. The patients were randomly divided into the study group or the control group according to the ratio of 1: 1. The treatment was single-blind for patients. The two groups of patients did not know the treatment method.

2.3 | Method

Debridement, washing and disinfection: the wounds in both groups were cleaned with normal saline, necrotic tissue and other foreign bodies were removed, blister fluid was introduced at a low level, and blister skin was preserved as much as possible. Dry the wound with sterile gauze.

Medication: the control group was treated with wet compress. The wound was covered with silver ion wet antibacterial biological dressing (Guangdong Taibao Medical Technology Co., Ltd.) and sterile gauze. The study group was treated with wet compress combined with chitosan wound dressing. Based on applying silver ion wet antibacterial biological dressing on the wound surface, chitosan dressing was added every time to cover the wound. Chitosan in the middle of the dressing clings to the wound. The dressings of the two groups were changed once a day in the first 3 days and once in the next 2 days. The treatment cycle is generally 3 to 4 weeks. When replacing, the wound should be cleaned again. If it is difficult to remove, it can be removed after wetting with normal saline. After the wound healed, both groups used German Monique scar patch (skin care) combined with elastic clothing or elastic bandage to continuously prevent scar hyperplasia.

2.4 | Material

Chitosan wound dressing was produced by Guangdong Taibao Medical Science and Technology Co., Ltd. The dressing was white or yellow film, which was suitable for isolating coating covers of traumatic wounds, surgical wounds and burn wounds, preventing infection, antibacterial wound protection and promoting wound healing. The dressing was made up of chitosan gel film, backing and paper. The chitosan gel film was made up of chitosan, polyvinyl alcohol, glycerin and pure water. The dressing was tested by Guangdong Medical Device Inspection Institute, China. The dressing was sterile, no Serratia marcescens growth, and the antibacterial rate against Escherichia coli and Staphylococcus aureus was above or equal 50%. It had good water resistance and long viscosity, and the chitosan content was 25% ~ 35%. According to GB/T16886.1-2011 biological evaluation requirements for medical devices, the dressing had grade 2 cytotoxicity in vitro and no delayed-type hypersensitivity reaction (Test report number: note 20 140 230).

2.5 | Outcome measurements

2.5.1 | Clinical data

The basic information of the two groups of patients was collected, including gender, age and burn area.

2.5.2 | Main outcome measures

Wound healing time. After removing the wound dressing, the wound base has been completely epithelized into the standard of wound healing.[7,8] Two deputy chief physicians of the burn department of our hospital observed the wound with naked eyes and jointly evaluated the wound under the condition of double blindness.

2.5.3 | Secondary outcome measures

Wound pain score: before treatment and 7, 14, 21, 28 days after treatment, the Faces Pain Scale-Revised (FPS-R) was used to score the wound pain of patients, with 1 points, occasionally feel pain, does not affect normal life; 2 points, the patients had pain, but can be slight activity, such as walking; 3 points, the patients had pain and could not exercise for a long time; 4 points, patients was with pain and unable to move except to the toilet; 5 points, patients with severe pain, unable to move.

Wound healing percentage: 14, 21, 28 days after treatment, the healing percentage was calculated. Healing percentage = healing cases/total cases × 100%.

Detection rate of wound bacterial culture: the basal secretions of the wound were taken for bacterial culture and drug sensitivity test on the 3rd, 7th and 14th day of dressing change, respectively. Bacterial positive rate = number of

bacterial culture positive cases / number of people in the group.

Treatment cost: It was calculated by dividing the total cost by the burn area.

Scar score: observe the scar growth 3 months after wound healing, and score the scar with Vancouver Scar Scale.

Incidence of adverse events and serious adverse events: serious adverse events refer to the events that require hospitalisation, prolong hospitalisation time, disability, affect working ability, endanger life or death and cause congenital malformations during the test.

2.6 | Statistical analysis

K-S test was used to test the normality of measurement data (test level $P = 0.05$), Levene method was used to test the homogeneity of variance between groups (test level $P = 0.05$), the data meeting the normal distribution and homogeneity of variance are expressed by "mean ± standard deviation", and t test was used to compare the measurement data between the two groups. The data that did not meet the normal distribution or homogeneity of variance are represented by the median, and the Mann Whitney U test was used for inter group comparison. The counting data were expressed by frequency and percentage. The comparison between the two groups adopted chi square test or continuity correction chi square test according to the theoretical frequency. Two-sided test was used for all statistics, and the test level was a = 0.05. When the results were $P < 0.05$, the difference was significant and statistically significant. SPSS 23.0 statistical software was used for statistical analysis.

3 | RESULTS

3.1 | Patient characteristics

A total of 80 patients with deep second-degree burns were included in the study. These were 40 cases of treatment group and 40 control group. There was no significant difference in demographic data, vital signs and baseline data between the study group and the control group at baseline, indicating that the two groups were comparable. (Table 1).

3.2 | Wound healing

The wound healing time of the study group and the control group were 19.53 ± 2.74 days and 24.78 ± 4.86 days, respectively. The wound healing time of the study group was shorter than that of the control group, and the difference was significant ($t = 3.571$, $P = 0.015$). The percentage of wound healing at the 14th after treatment in the two groups was significant ($X^2 = 6.054$, $P = 0.014$), and that in the study group was higher than that in the control group (65.00% versus 37.50%). There was no significant difference in the percentage of wound healing between the two groups on day 21 and 28 after treatment. (Table 2).

3.3 | Pain score and scar score

There was no significant difference in pain scores between the two groups at each time point. (Table 3) The scar growth was observed 3 months after wound healing. The scar score of the study group was 6.00 ± 0.98, and that of the control group was 8.77 ± 1.19. The three-month scar score in the study group was significantly lower than that in the control group ($t = 2.571$, $P = 0.031$). It indicated that the scar hyperplasia in the experimental group was better than that in the control group 3 months after wound healing.

3.4 | Bacterial culture

The detection rate of wound bacterial culture in the study group showed a downward trend. That of the control group showed a fluctuating trend. There was no significant difference in the detection rate between the two groups on the third day. The positive rate of wound secretion culture on the 7th and 14th day was statistically significant ($X^2 = 4.528$, $P = 0.033$; $X^2 = 6.646$, $P = 0.010$), and the study group was lower than the control group (29.03% versus 81.82%; 8.11% versus 42.86%). (Table 4).

3.5 | Treatment costs and incidence of adverse events

The treatment cost was 1258.7 ± 223.6 RMB in the study group and 1248.9 ± 182.3 RMB in the control group. There was no significantly difference in the tow group ($t = 1.571$, $P = 0.071$). o adverse events or serious adverse events occurred in the two groups.

4 | DISCUSSION

The main purpose of burn treatment is to promote wound healing as soon as possible to reduce the occurrence of

TABLE 1 Comparison of baseline data between study group and control group

	Study group (n = 40)	Control group (n = 40)	$t/X^2/U$	*P*
Sex (male/female)	23/17	21/19	$X^2 = 0.202$	0.653
Age (years)	38.12 ± 7.64	41.83 ± 9.32	$t = 0.756$	0.126
Weight (kg)	65.92 ± 8.74	64.34 ± 9.99	$t = 0.406$	0.656
Height (cm)	170.21 ± 6.42	168.27 ± 7.43	$t = 0.866$	0.722
Body temperature (°C)	36.23 ± 0.36	36.57 ± 0.22	$t = 0.665$	0.537
Respiratory rate (times/min)	19.86 ± 1.33	19.65 ± 1.21	$t = 0.535$	0.238
Burn surface (cm^2)	14(2,30)	12(2,25)	U = 390.5	0.377
Burn site			$X^2 = 0.202$	0.432
Limbs	11	14		
Trunk	19	14		

TABLE 2 Comparison of wound healing time and healing percentage at different time points after treatment between the two groups

Group	Wound healing time	14 days	21 days	28 days
Study group (n = 40)	19.53 ± 5.74	65.00% (26/40)	97.50% (39/40)	100% (40/40)
Control group (n = 40)	24.78 ± 4.86	37.50% (15/40)	95.00% (38/40)	100% (40/40)
t/X^2	$t = 3.571$	$X^2 = 6.054$	-	-
P	0.015	0.014	-	-

TABLE 3 Wound pain scores of the two groups at each time point

Group	Before treatment	7 days	14 days	21 days	28 days
Study group (n = 40)	4.57 ± 0.85	3.44 ± 0.61	3.12 ± 0.37	1.65 ± 0.70	0.29 ± 0.16
Control group (n = 40)	4.62 ± 0.76	3.52 ± 0.64	3.18 ± 0.42	1.36 ± 0.37	0.31 ± 0.22
t	0.761	0.871	0.041	1.280	0.655
P	0.544	0.221	0.761	0.801	0.811

TABLE 4 Results of bacterial culture (positive/negative)

Time	Study group (n = 40)	Control group (n = 40)	x^2	*P*
3 days	11/29	9/31	0.267	0.606
7 days	9/31	18/22	4.528	0.033
14 days	3/37	12/28	6.646	0.010

infection and improve the appearance and function after healing. Early treatment of burn wounds includes debridement and topical dressing prevention. Early and correct treatment is the key factor of burn wound healing. The healing principle of deep second-degree wounds is mainly connective tissue remodelling, which relies on epithelial cells and residual skin appendages to form skin islands, crawls to the surrounding wounds and gradually covers the wounds. Retain necrotic epidermis, prevent infection, protect residual epithelial tissue and reduce scar formation.[9]

Chitosan is a semi synthetic organic polymer with unique chemical structure, which is widely used in biomedical field because of its good biocompatibility, biodegradability, biosafety and low toxicity.[10] The molecular structure of chitosan dressing is similar to that of mucopolysaccharide matrix in the intercellular matrix, with good cell compatibility, which provides a favourable environment for the growth of skin cells and is conducive to wound healing.[5] The positive charge on the surface interacts with the negative charge on the surface of red blood cells, resulting in the agglutination and adhesion of the wound interface and the rapid closure of the bleeding point. Chitosan has high affinity for human tissue. N-phthalocyanine glucosamine is the basic component of hyaluronic acid and an important matrix of human body.

It is used in human wounds, various wounds and ulcers, without any rejection, and can promote the production of collagen and wound healing.[11] The moisturising property of chitosan dressing makes it difficult for wound exudate to form dry scabs, while the self-soluble debridement of chitosan makes necrotic tissue easy to fall off[12] It is easy to remove during dressing change and has little irritation to the wound. Deep second-degree wound does not form dry scabs, and necrotic tissue dissolves quickly. The residual island under the scab is retained to a large extent, which is conducive to the closure of the wound after the dissolution of necrotic tissue and improve the quality of healing. Wound repair requires calculating the release of inflammatory cells and inflammatory factors. However, the excessive inflammatory reaction after burn damages the surrounding healthy tissues and aggravates the local tissue damage. Therefore, chitosan can absorb osmotic fluid and a large number of inflammatory factors,[13] avoid the aggravation of wound injury, buffer the inflammatory reaction of the wound, so as to create a relatively mild growth environment, which is more conducive to the growth of vascular endothelial cells. In addition, chitosan dressing can also stimulate cell proliferation and promote wound healing by reducing local oxygen tension, promoting angiogenesis and growth factors in contact with the wound.[14] In this study, the wound healing speed of the study group was significantly faster than that of the control group, indicating that chitosan dressing has a significant role in promoting wound healing. It is consistent with the research results of Shi et al.[15]

In the traditional burn dressing change method, multi-layer sterile gauze is used to cover the wound to drain the wound exudate and prevent wound infection. However, there is a large amount of exudate during the exudation period, and the contact layer of the dressing is difficult to observe and keep dry, which is easy to cause bacterial infection such as Pseudomonas aeruginosa. After the wound is soaked in exudate, the hard skin or eschar is not easy to dry, resulting in increased infection and tofu like necrosis. If the dressing is changed every day, the workload of doctors will increase. Chitosan wound dressing should have the ability to effectively manage wound exudation. Effectively absorb wound exudates, maintain a moist environment, manage the moist environment, and promote wound healing. It is not only convenient for clinicians to use, but also can effectively control bacterial infection.[16] In this study, the positive rate of bacterial culture of wound secretion in the study group was significantly lower than that in the control group on the 7th and 14th days after treatment. The results are similar to those of Liu et al[17]

After burn, the original tissue is destroyed, the structure is disordered, and the continuity and stability of the skin are damaged. Therefore, the wound cover requires that the wound can be attached at the same time, and will not cause secondary damage to the wound when changing the dressing. The moisturising property of chitosan dressing makes it difficult for the wound exudate to form dry scabs and is not easy to cause wound adhesion. During the dressing change, the pain can be reduced. Only after the dressing reaches the upper limit of absorption, it is necessary to replace the dressing in time to avoid wound deposition. Keeping the wound relatively clean is more conducive to wound healing. In addition, silver ion wet antibacterial biological dressing can continuously release silver ions, play an antibacterial and synergistic role, and promote the rapid healing of wound.[18] As the control group did not use gauze to wrap the wound, there was no significant difference in dressing change pain scores between the two groups. There were no adverse events or serious adverse events during the treatment, which met the safety requirements of clinical use.

The limitations of this study mainly include the following aspects. First, the limitations of experimental design. Due to the need to tell the patients and their families about the disease and dressing characteristics in detail during the clinical treatment, it is sometimes difficult to achieve double-blind observation. Second, the characteristics of the dressings used in this study determine that the amount of leachate absorbed by the dressings is limited, which is not as good as that of foam dressings. It needs to be replaced in time during the exudation period to avoid infection caused by the outflow of leachate. Third, this study is a single-center study, selection bias is inevitable.

5 | CONCLUSION

The results showed that chitosan dressing had a good effect on burn and scald wounds. It can significantly shorten the time of wound healing, reduce wound pain and wound infection, and effectively improve scar hyperplasia. It meets the requirements of safe and effective clinical use, and is worthy of clinical application.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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How to cite this article: Hu J, Lin Y, Cui C, et al. Clinical efficacy of wet dressing combined with chitosan wound dressing in the treatment of deep second-degree burn wounds: A prospective, randomised, single-blind, positive control clinical trial. *Int Wound J*. 2023;20(3):699-705. doi:10.1111/iwj.13911