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Original Article

Evaluation of the efficacy of Agicoat in the treatment of partial-thickness skin graft donor sites of burn patients

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Abstract: Introduction: Burns is the most common condition that requires extensive skin grafting. Treatment of burns is associated with long hospital stays, expensive medications, multiple surgeries, and long-term rehabilitation. Rapid healing of skin donor areas in partial-thickness burn wounds is important for the patient. Partial-thickness skin grafting is a technique that can reduce healing time and improve the treatment. Nanocrystalline silver contains antibacterial and anti-inflammatory properties. This study aimed to evaluate the efficacy of Agicoat in the treatment of partial-thickness skin graft donor sites of burn patients in terms of healing time, pain and scarring. Method: This clinical trial study was performed on 100 patients who burn and were referred to Imam Khomeini Hospital in Tehran from July to January 2020. Patients with second- and third-degree burns who had burned 10 to 30 percent of their body surface and required partial-thickness skin graft surgery, were considered for this study. Each patient was compared to herself. The skin donor site was then randomly divided into three parts A, B and C and each part was dressed with Agicoat™, Mepitel and Vaseline gauze. On days 4 and 8, the amount of pain when changing the dressing was recorded based on visual analog scale (VAS). After six months, the patients were evaluated and compared for the scarring site based on Vancouver Scar Scale (VSS). Result: Comparison of the average healing time between groups showed that the average healing time in both groups was significantly shorter than the Vaseline group (P=0.005). Comparison of wound pain between groups on Day 4 showed that the mean pain in the Agicoat group and also the Mepitel group was significantly lower than the Vaseline group (P=0.004). However, Agicoat and Mepitel groups did not show a significant difference. Also, a comparison of pain between groups on Day 8 and the mean VAS six months after skin graft showed no difference between groups. Conclusion: According to the findings of this study, if the Agicoat dressing is cost-effective, it can be a good alternative to cover the wound of the skin donor site, and it heals faster and reduces pain.

Keywords: Burn, skin graft, Agicoat

Introduction

Skin grafting is a very common procedure in plastic surgery and is used to treat skin defects after trauma, infection, removal of benign and malignant tumors, and adhesions after various diseases. Burns is the most common condition that requires extensive skin grafting [1, 2]. Every year millions of people are injured by burns. Treatment of burns is associated with long hospital stays, expensive medications, multiple surgeries, and long-term rehabilitation [3, 4]. Healing the burn wounds and the site of the skin excision for skin grafting as soon as possible, in addition to reducing the complications, pain and cost, achieve better cosmetic results and performance. Burn wounds and skin graft donor sites have a higher chance of infection due to the extent and accumulation of dead tissues as well as the compromised immune system and are the most common cause of death in less developed countries [4-7]. For this reason, burn tissue excision and early skin grafting as the best treatment for burns, not only reduces mortality but also has better cosmetic and functional results. However, this method has its disadvantages and advantages and must be considered when making decisions [2, 7-9]. The second wound that occurs to create a partial-thickness skin graft is a donor site wound. This secondary wound is very important in terms of healing time, pain, scarring, and cosmetic results [9-11]. Also, if donor sites heal quickly, can be

reused in cases of burns or extensive tissue loss [12, 13]. Therefore, any technology that reduces the healing time of the donor site is important [2, 13, 14]. The donor site area for partial-thickness graft lacks epidermis and variable depth of dermis, and healing of this area is possible only with epithelialization. The dressing material for the skin graft donor sites should have the characteristics of being able to create a suitable environment for epithelialization, prevent infection, reduce discomfort and pain, absorb the exudates, be easily applicable and cost-effective [15-17]. The partial-thickness skin graft donor sites are expected to improve within 7 to 10 days with proper care and conditions [14-16]. Recently, due to a better understanding of the factors affecting wound healing, new dressing materials with modern technology have been produced. However, the most ideal dressing for partial-thickness skin graft donor areas is not yet produced [18, 19]. One of the silver products that are widely used in terms of covering traumatic injuries, burn wounds, diabetic wounds, skin grafts, incision and minor scratches are silver dressings, which are used in various forms such as topical creams, emulation, catheters, and prosthesis [20-22]. Nanocrystalline silver has been used for this purpose for several years and has had better results in preventing infection, although its side effects should be considered, especially the accumulation in various tissues of the body. The effectiveness of a silver nanoparticle-coated polyethylene mesh in preventing infection in burn wounds has been proven [23-25].

Although the exact anti-inflammatory mechanism of silver nanoparticles is not clear, because the important cause of inflammation is the infiltration of neutrophils and matrix metalloproteinases (MMPs) and the level of MMPs is reduced by the use of nanocrystalline silver and their derivatives, it is expected that this dressing can suppress the activity of this enzyme and reduce the inflammation. The specified properties of silver nanoparticles contain antibacterial properties, anti-inflammatory and antifungal effects, environmentally friendly, non-allergic and non-stimulating, heat resistance, lack of resistance to microorganisms and high stability [3, 19, 23]. Silver dressings like Acticoat™ (Smith & Nephew, Inc., Largo, FL), a nanosilver-coated high-density polyethylene mesh and silver oxide by a physical vapor deposition technique, Silverlon™ (Argentum LLC, Chicago, IL), and Agicoat™ (Emad pharmaceuticals Co., Esfahan, Iran)-a nylon fabric coated with silver nanoparticles by using a chemical wet deposition method (CWD), are among the metallic dressings used [24, 26, 27]. Agicoat™ is a single-layer dressing coated with nanocrystalline silver in which silver is deposited on highly flexible nylon fibers mesh by using a CWD method. This layer exerts its antimicrobial and anti-inflammatory effects by slowly releasing Ag ions. This study aimed to evaluate the efficacy of Agicoat in the treatment of partial-thickness skin graft donor sites of burn patients in terms of healing time, pain and scarring.

Methods and material

Study design

This clinical trial study was performed on 100 patients who burn and were referred to Imam Khomeini Hospital in Tehran and Azar clinic in Abadan from July 2017 to January 2020. Patients with second- and third-degree burns who had burned 10 to 30 percent of their body surface and required partial-thickness skin graft surgery, were considered for this study. The study protocol was approved by the Research Committee of Tehran University of Medical Sciences and the Ethics committee has confirmed it (Ethics code: IR.TUMS.MEDICINE.REC.1392.207, Iranian Registry of Clinical Trials (IRCT) code: IRCT2018988173N2). Written informed consent was obtained from all patients to participate in the study.

Inclusion and exclusion criteria

Due to the different dressings for the skin graft donor sites, it was not possible to perform the study with the blinded procedure to evaluate the healing phase, but it was possible for the site scarring. Inclusion criteria included adults between 18 and 65 years of age, second- or third-degree burn wounds, a total burn surface area was between 10 and 30%, no comorbidities, no medication, and all patients were under their control. Exclusion criteria were silver sensitivity as well as infection of the wound site.

Procedure

In all patients after anesthesia, the skin required for skin grafting was harvested in a standard manner from the posterior or anterolateral zone of the thigh by an electric dermatome and with the same thickness.

The skin donor site was then randomly divided into three parts A, B and C and each part was dressed with one of three types of dressing. Part A was dressed with Agicoat, part B with Mepitel, and part C with Vaseline gauze. The dressing of all patients was changed every four days and the wound was observed by two people (a burn surgeon and a wound nurse) and the amount of healing was recorded based on the percentage of epithelialization and a photograph was taken. Inchoate skin graft was determined by two expert plastic surgeons based on the proper vascularization and attachments to the graft bed.

Assessments

On days 4 and 8, the amount of pain when changing the dressing was recorded based on visual analog scale (VAS). Based on VAS, the pain of the patient is scored from 0 (least pain) to 10 (highest pain). Also, after six months, the patients were evaluated and compared for the scarring site based on Vancouver Scar Scale (VSS). VSS is widely used in clinical practice and research to document changes in scar appearance. Based on VSS, the scar is evaluated for pigmentation (2 scores), vascularity (3 scores), pliability (5 scores) and height (3 scores) and is scored from 0 (normal score) to 13 (worst condition). In all patients, the last layer of dressing adhered to the wound was not replaced until epithelialization was complete. In cases of suspected skin graft donor site infection due to discharge, odor, abnormal pain or discoloration, the dressing was completely removed and after getting a surface culture, the dressing was changed daily and the patient was excluded from the study.

We also assessed patient's quality of life using a questionnaire. A 36-Item Short Form Survey (SF-36) was also filled for each patient. This questionnaire is an oft-used, well-researched, self-reported measure of health covering eight domains of health [28]. The SF-36 is used to indicate the health status of particular populations, to help with service planning and to measure the impact of clinical and social interventions.

Statistical analysis

After collecting the study data, they were entered into SPSS software (version 25, IBM Corporation, Armonk, NY) and analyzed. All data were expressed as mean ± SD. Because the variables do not follow a normal distribution, Kruskal-Wallis test was used for comparison between groups and Mann-Whitney U test and the Independent samples t-test were used for paired sample comparison.

Result

Study population and healings

In this study, 100 patients (80 men and 20 women) were studied. The mean age of patients was 38.10±17.54 years. The mean healing time was 13.20±1.93 days in the Agicoat group, 15.20±2.52 days in the Mepitel group and 16.80±2.52 days in the Vaseline gauze group. Overall comparison between the groups showed that the difference was significant (P=0.011). Paired comparison of the mean healing time between groups showed that the average healing time in the Agicoat group was significantly shorter than the Vaseline group (P=0.005). But no significant difference was observed in the pairwise comparison between other groups (A to B and B to C). Photographs of wound healing on different days and groups of two patient samples are presented (**Figure 1**).

Further assessments

The mean pain of the skin donor site after two measurements is summarized in **Table 1**. Comparison of wound pain between groups on Day 4 showed a significant difference (P= 0.003). Comparison between groups showed that the mean pain in the Agicoat group was significantly lower than the Vaseline group (P=0.004). Also, the mean pain of the Mepitel group was less than the Vaseline group with a significant difference (P=0.002), but Agicoat and Mepitel groups did not show a significant difference. Comparison of pain between groups on Day 8 showed no difference between groups. The results of mean VAS six months after skin grafting showed that the mean of VAS was 8.16±2.71 in the Agicoat group, 6.1±66.63 in the Mepitel group, and 7.66±2.80 in the Vaseline gauze group, and the difference between the groups was not significant.

We also indicated that after treatments, the mean SF-36 score was 75.2±11.57 in the Agicoat group and 70.3±10.95 in the Mepitel

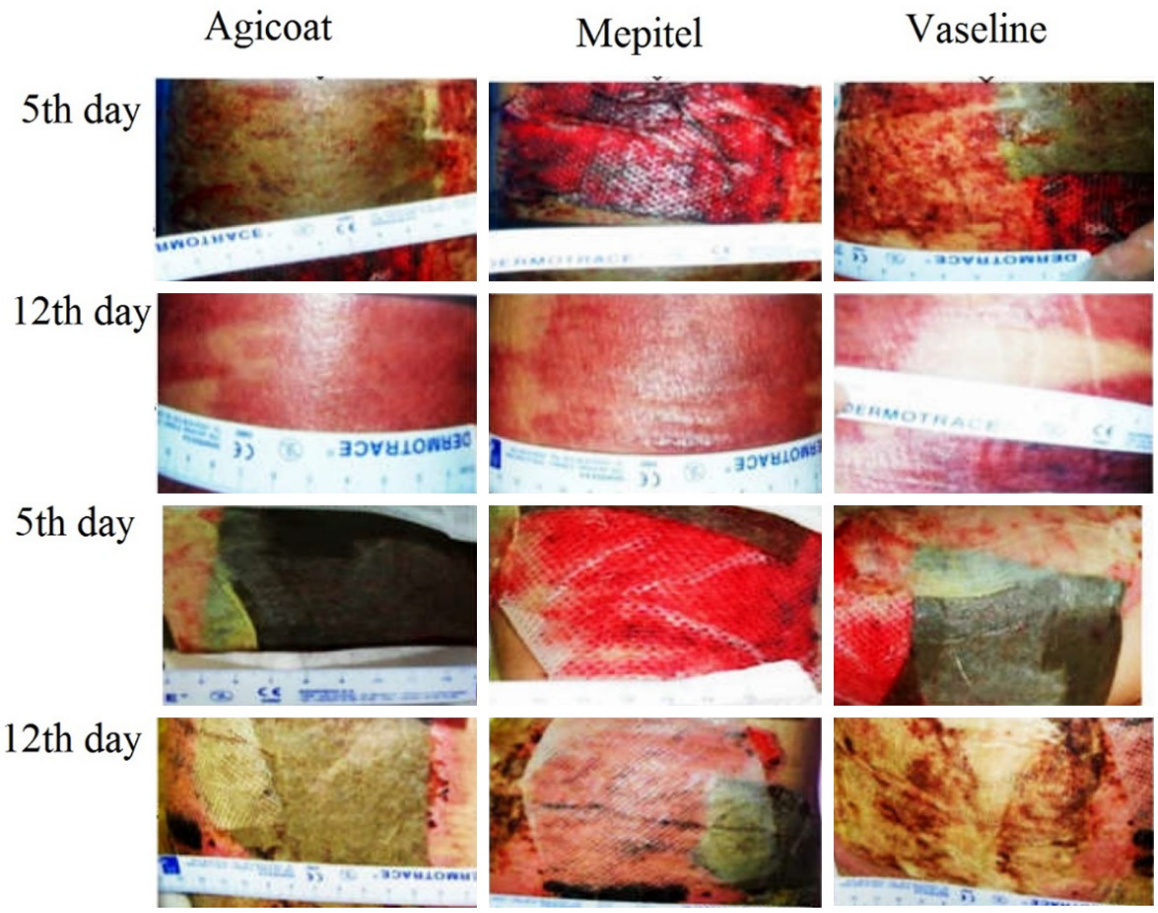

Figure 1. Comparison of wound healing in three groups in both samples.

Table 1. Mean pain of the patients during the study

Groups	Day	Minimum	Maximum	Mean	Standard deviation
Agicoat	4th day	4	9	6.70	1.56
	8th day	3	8	5.80	1.39
Mepitel	4th day	5	9	6.50	1.17
	8th day	4	9	6.00	1.33
Vaseline	4th day	7	10	8.70	1.05
	8th day	5	9	7.20	1.54

group (P=0.02). But we should note that both groups had a significant increase in the SF-36 scores compared to the beginning of the study (P<0.001). These data are shown in **Table 2**.

Discussion

A comprehensive systematic review and meta-analysis show that the use of nanocrystalline silver dressings reduces the length of hospital stay, reduces pain, requires less surgery, and reduces the rate of infection compared to silver sulfadiazine/silver nitrate [18]. The aim of this study was to evaluate the non-infection partial-thickness skin graft donor sites in terms of speed of healing and the pain and scarring, so the wound was not infected.

Agicoat nanocrystalline silver dressing is a single-layer dressing coated with nanocrystalline silver in which silver is deposited on highly flexible nylon fibers mesh by using a CWD method [19]. This layer exerts its antimicrobial and anti-inflammatory effects by slowly releasing Ag ions [20]. The results of the present study showed that Agicoat causes faster healing with less pain and is similar to Mepitel and better than the traditional method. But the scarring did not differ in the three groups.

Adhya and others concluded that burn wound healing with nanocrystalline silver was faster

Table 2. Assessments of SF-36 score in patients

		Agicoat	Mepitel	Vaseline	*P*-value[1]
SF-36 score*	Before	61.3±5.66	60.28±7.18	61.39±6.12	0.754
	After	75.2±11.57	70.3±10.95	68.25±11.57	0.02
	P-value[2]	<0.001	<0.001	<0.001	

*Data is represented by mean ± SD; *P* value[1]: between group analysis; *P* value[2]: within group analysis using Mann-Whitney U test and Independent samples t-test.

than silver sulfadiazine, and indicating a reduction in the defect of silver compounds using nanoparticles [21]. It has also been shown in some studies that silver nanocrystalline compounds with biocompatible nanofibers can achieve faster healing. The findings of these studies are consistent with the results of the present study that Agicoat causes better healing. In a study by Liu and colleagues, nanocrystalline silver caused more granulation, increased epithelialization, higher keratinocyte activity, and reduced inflammation, all of which improve wound healing. In addition, the antimicrobial properties of silver make it advisable to use for any wound, provided it is affordable [22].

In a comparison between Acticoat and Aquacel Ag, Verbelen and colleagues stated that both silver dressings had similar results in terms of healing time and bacterial control, but Aquacel Ag dressings significantly increased patient and nurse comfort and were indicated to be significantly cost-effective than Acticoat dressing [23]. In the present study, Agicoat was cheaper than Mepitel. Healing time is one of the primary consequences. Faster re-epithelialization allows us to reuse the skin donor site, and this is especially important in extensive burns where there is a lack of skin donor site. In the current study, traditional methods have been used but it is like the Mepitel without nanocrystalline silver. Therefore, the determining factor in choosing between these two dressings will be the cost. One of the advantages of Agicoat is the small pores on the dressing, which due to their size allow exudate and water vapor transmission but prevent microbial organisms transmission. This dressing does not adhere to the wound and does not insert to the re-epithelialization of the wound donor site during replacement. In addition, other properties of this dressing, such as providing a moist environment, antimicrobial properties, non-adhesion and replacement reduction, reduce the length of epithelialization and hospital stay.

Pain is considered as one of the most common complaints in patients with graft donor sites after surgical treatment of burn wounds, which often eliciting more pain than the receiving sites [25]. One of the goals of dressings is to reduce the severity of pain in the donor site after surgery. The dressings used in this study, due to their non-stick properties, cause minimal damage to donor sites and replacement reduction and reduce pain after surgery. In the present study, the pain score was significantly reduced compared to the control group ($P< 0.05$). Consistent with these results, Khandelwal and others found that patients in the silver dressing group did not experience the pain that patients in the control group experienced when changing a dressing.

There was no significant difference in the examination of the scarring after six months, and therefore the aesthetic results did not improve with nanocrystalline silver or new dressings such as Mepitel, although the small sample size makes the conclusion ambiguous.

Conclusion

According to the findings of this study, if the Agicoat dressing is cost-effective, it can be a good alternative to cover the wound of the skin donor site, and it heals faster and reduces pain. It is suggested that this study be conducted with a larger sample size so that if the results are positive, this dressing produced in Iran can be replaced by expensive foreign dressings.

Disclosure of conflict of interest

None.

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