

Evaluation of the therapeutic effect of dressing containing Silver in the process of healing skin blisters caused by limb fractures

Abstract:

1.Introduction:

The main activity of the skin is to create a protective barrier against damage caused by contact with the environment around the body. Loss of a large portion of the skin due to injury or disease and failure to regenerate the affected area may result in disability, infection, or even death. Recent advances in life sciences have made it possible to understand the effective processes in wound healing and to take effective steps towards better wound care. A number of studies have shown that immune cell infiltration and messaging play a key role in scar formation and fibrosis [1, 2]. Each year in the United States, more than 1.25 million people suffer from burns, and 6.5 million people suffer from bed sores, circulatory ulcers due to cessation of circulation or diabetes, or fracture injuries [3]. Wound healing is a vital process for humans and many animals. One of the important goals of skin wound care is the process of rapid wound closure [4].

Open fractures due to severe soft tissue disorders that may lead to devastating complications are considered an orthopedic emergency. On the other hand, closed fractures, especially fractures caused by high-energy mechanisms, are often associated with severe soft tissue injury. Soft tissue damage, especially skin damage as the first skin defense barrier can have a negative impact on the final outcome of patients. Fracture blisters, in particular, develop as a sign of significant tissue damage and appear between 6 to 72 hours after injury. They can delay the treatment of definitive fractures for a considerable time and at the same time increase the risk of postoperative wound complications [5]. Fracture blisters are a relatively uncommon complication of parts of the body, such as the ankle, wrist, and foot, where the skin adheres tightly to the bone and is protected by a small amount of subcutaneous fat. The blister is similar to a second-degree burn. These blisters significantly alter the treatment and make it difficult to splint or cast. These blisters are often placed on surgical incisions. Past studies have shown no consensus on the management of this fractured skin blister. However, most authors agree on initial treatment before blistering or delayed blistering before surgery. [6].

In recent years, dressings with different compositions have been introduced to protect and accelerate the healing of skin damage caused by burns, fractures and other accidents leading to skin damage. Recently, bacterial cellulose (BC) has been

used in dressings to reduce the duration of wound healing [7, 8], however, more recent studies have shown that BC alone has no antimicrobial activity [9]. In general, inorganic nanomaterials play an important role in antibacterial applications due to their large area and particle shape properties [10]. Metal nanoparticles and metal oxides, which are well known for their antibacterial properties, include silver (Ag), titanium oxide (TiO₂), copper oxide (CuO) and zinc oxide (ZnO). Like other polymeric materials, BC can be used to make composites with metals and metal oxides through various synthetic methods [11, 12]. Numerous studies have shown that BC / Ag composite has antibacterial activity against gram-positive and gram-negative bacteria [13, 14]. Some previous studies have reported the synthesis of GO-Ag nanocomposite and its antibacterial activity [15]. The benefits of silver are known as an antimicrobial agent. Various silver-containing dressings are now used to treat wounds. Acticoat is a nanocrystalline silver dressing that was introduced in the late 1990s and has been developed to overcome some of the defects of older dressings with continuous silver release for up to 7 days. Studies show that Acticoat has better antimicrobial activity than silver dressings, also has fewer side effects, and reduces recovery time [16].

In a comparison between Ag Aquacel and Acticoat, Verbelen et al. stated that both silver dressings had similar results in terms of healing time and bacterial control, but Ag Aquacel dressings significantly increased patient and nursing comfort and significantly It was shown to be significantly cheaper than Acticoat dressing [17].

Cotton gauze is one of the most successful wound dressings that uses the inherent properties of cotton fibers. Modern wound dressings require other properties such as antibacterial and moisture retention. One study shows that conventional cotton gas treatment with Ag nanocomposite has the ability to care for wounds due to the properties of modern dressings to heal wounds. Chitosan has been used as one of the natural polysaccharides in a study of dressing compounds. The antibacterial amounts of cotton gas combined with chitosan / Ag / ZnO are higher than other dressings, indicating a synergistic effect on the nanocomposite. Chitosan is / Ag / ZnO. Cotton gas treatment with chitosan / Ag / ZnO nanocomposite also increased drying time and water absorption, which is one of the main indicators of modern wound dressing [18].

Recent studies were reported the effect of dressing containing Silver on the healing process of burn wounds, healing at the skin graft site, reduce the risk of infection

and hospitalization, and its cost effectiveness. The present study aimed to investigate the effect of Agicoat silver Nano-Crystalline Dressing dressing, produced by Emad Pharmaceutical Company, on blisters caused by bone fractures.

2.Method and Material:

2.1.Patient celection:

This a **prospective study** conducted according to the guidelines of the Ethical Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1401.025). Eligible patients attending the Orthopedic Clinic of Isfahan Research Center, Isfahan, Iran, between **2021**, and **2022**, were randomly assigned.

2.2. Inclusion and exclusion criteria:

The inclusion criteria included all patients with blister due to bone fracture, aged between 18-65 and Consent to participate in the study.

The exclusion criteria included Sensitivity to silver , Amputation indication , patients who did not agree to participate in the study and those who did not participate in the study until the end and did not come for follow-up sessions.

The patients were fully informed about the risks, advantages and the trial process. The informed consent was taken from those patients who met the following requirements. They had been diagnosed after a first admission to the Kashani Hospital. They were aged between 18 and 65 years with non-healing blisters that had created due to bone fracture and ulcer sizes between **???** and **???** cm²; all blisters were located on the leg and foot; finally, the patients read, comprehended and signed the informed consent specific to the study.

The patients were simply randomized into 2 groups; in group A, they were treated with Agi Coat dressing and in group B, they were treated with Gaz Vaseline for coating the blister. Agi coat dressing, which used in this study, was produced by Emad Pharmaceutical Company, Razi industrial zone, Isfahan, Iran. This dressing is a single-layer dressing with a coating of silver nanocrystals, which are coated by the chemical reduction method, silver on a network of nylon fibers with very high flexibility. This layer exerts its antimicrobial and anti-inflammatory effects by slowly releasing silver ions.

The blisters were also divided into Hemorrhagic and non-hemorrhagic groups.

۲/۳.How to use the dressing:

The wound or burn site was cleaned with distilled water, betadine, burn ointment, etc. The dressing was removed from the package and moistened with distilled water. The excess water was taken from the dressing and placed directly on the wound, so that the side was placed at least one centimeter outside the wound. Then another absorbent dressing was placed on the back and finally it was fixed at the wound site with a simple bandage, tape or glue.

2.3. Evaluation of blisters

The blisters were dressed by Agi coat once a week and every day with Gaz Vaseline, and were followed up in day 7 and 14. On all days of hospitalization and clinic visits in both groups, an orthopedic surgeon and a wound specialist visited the patients. The amount of pain, duration of visit (measured by minutes) and general condition of the wound was checked. Photography was done on the first, seventh and fourteenth days after the first day of dressing. Photographs were taken on all days for all patients by one photographic camera, lens perpendicular to the wound and at a distance of fifteen centimeters from the wound. The pictures of wounds were analyzed by a medical doctor with Mosaic soft ward.

Result:

A total of 31 participants have been examined in the study. The participants in this study were in two Ag coat groups with 16 participants and Gaz Vaseline group with 15 participants. Table 1 shows the demographic characteristics of the study subjects.

Table 1 compares the demographic characteristics of the participants according to the study groups. As the results of the table 1 show, there was no significant difference between the mean of age and BMI and frequency of gender in the two study groups ($P>0.05$).

In table 2 we compared duration of visit, number of dressing, net cost of dressing and hemorrhagic wounds between groups. As the results of table 2 show, there was significant difference mean between duration of visit, number of dressing and net cost of dressing ($p< 0.05$) , we expect that healing was considered complete

sooner when the blister is non- hemorrhagic, but hemorrhagic and non-hemorrhagic wounds did not have any significant difference between two groups.

In macroscopic study and analysis for evaluation and comparing wound area with the Mosaic soft ward, there were significant relation in time ($p_1=0.00$). There is no significant difference between the groups($p_2=0.84$). There was significant difference between time and group($p_3=0.00$). In day 14 the wound area between groups had significant difference($p_4=0.00$). (table3) In VAS score there were significant difference in time, group ($p_{1,2}=0.00$), there was no significant relation between time and group($p_3=0.62$). In all days the wound area between groups had significant difference($p_4=0.00$). (table3)

Discussion :

In this study, the patients which their blisters dressed with ag coat dressing had significantly less pain during the time and between groups in compare with gaz vaselin group, which was measured by VAS score. Also, in ag coat group the wound healing was significantly faster during the time and in the presence of both groups, which was measured by analyzed the wound area with the Mosaic soft ward. Duration of visit and the usage of number of dressing was significantly less in ag coat group in compare with gaz vaselin group.

A comprehensive systematic review and meta-analysis shows 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 another kinds of dressing [19]. As the same, in our study also the pain , hospitalization length was less in ag coat group and non of our patients had infection.

In another study, similar to our study, the rate of healing and pain with silver nanocrystal dressing (single-layer dressing) with a coating of silver nanocrystals by chemical reduction method, silver on a network of nylon fibers with the flexibility of this layer with release Slowly silver ions [20] are coated very highly (the results of the study [21] exert their antimicrobial and anti-inflammatory effects) and

showed that Ag coat produces faster healing with less pain and is better than the traditional method like gaz vaselin [22].

In one study, a comparative evaluation of two types of burn wound treatment was performed. To perform this evaluation, patients with partial thickness of burn wounds with a total body area <40 were randomly treated with nanocrystalline silver nylon wound dressing or silver sulfadiazine cream. The effectiveness of treatment, the use of analgesics, the number of wound dressings changed, wound infection and the final cost of hospitalization were evaluated. Exactly similar to our study, this study showed that silver nylon wound dressing reduces the length of hospital stay, analgesia, wound infection and inflammation compared to another kinds of dressing [23].

In the study of Adhya et al., The healing of burn wounds with silver nanocrystals was faster than other dressing, which showed an increase in the healing effect of silver compounds using nanoparticles [24]. Some studies have also shown that compounds. Silver nanocrystals with biocompatible nanofibers can provide faster healing. Liu et al. Reported that the presence of silver nanocrystals increased granulation, increased epithelialization, increased keratinocyte activity, and reduced inflammation, resulting in better wound healing. In addition, the antimicrobial properties of silver make it advisable for any wound, provided It is affordable in terms of price [25].

The mentioned studies and other studies in this field have examined the antimicrobial properties of Agicoat silver Nano-Crystalline Dressing due to its properties such as induction of tissue granulation, increased epithelization, increased activity of keratinocytes, reduced inflammation [25] and reduced pain [26], and in order to its cost-effectiveness, it is recommended for any casualty.

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Table1: Clinico-demographic patient characteristics

Type of dressing		Agi Coat(16)	Gaz Vaseline(15)	p-value
Demographic variables				
Age(mean±SD)		40.93±6.71	40.73±6.00	0.93
BMI(mean±SD)		24.07±0.61	23.83±0.58	0.28
Gender n(%)	Femal	8(50)	8(46.7)	0.56
	mail	8(50)	7(46.7)	

Table 2:

		Ag coat(16)	Gaz vaseline(15)	
Duration of visit(min/day)		16.68±4.19	27±7.02	0.00
Number of dressings(mean±SD)		3±0.00	433.46±14.15	0.00
Net cost of dressing(Rial)		2425361.25±938118.7564	8693333±2830312.115	0.00
Hemorrhagic N(%)	Hemorrhagic	8(50)	9(60)	0.42
	Non-hemorrhagic	8(50)	6(40)	

Table3. Summary of analysis of repeated variance for the average of wound size in treated and control group

		Day0	Week1(day7)	Week2(day14)	P1(time)	P2(group)	P3(time*group)
Wound area(cm ²)	Agi coat	23.43 ±9.93	20.65 ±9.61	17.01±9.18	0.00	0.84	0.00
	Gaz Vaseline	27.28 ±10.89	26.88 ±10.86	26.44 ±10.82			
P4		0.31	0.10	0.01			
Vas Score	Agi coat	5.34±0.78	3.96±0.80	2.56±0.60	0.00	0.00	0.62
	Gaz Vaseline	7.70±0.88	6.50±0.96	5.13±0.93			
P4		0.00	0.00	0.00			

P1, P2 and P3 based on repeated measure ANOVA and P4 based on sample T-test, all variables are presented as mean± SD

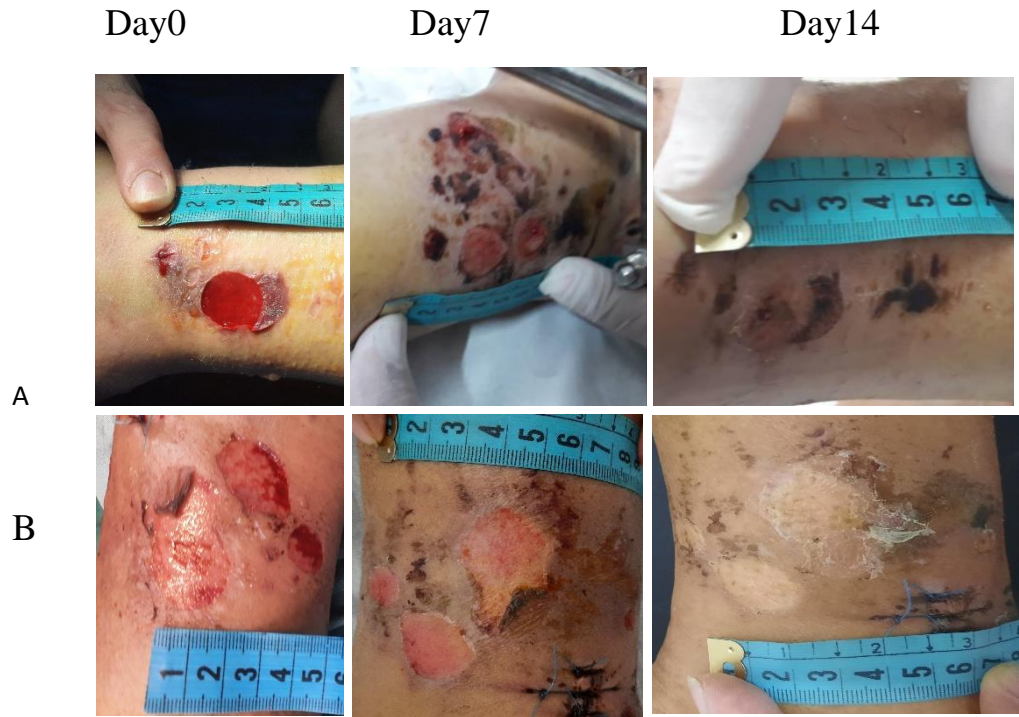


Figure1: macroscopic view of the blisters and healing process based on dressing type.(A: Ag coat, B: Gaz Vaseline)