Effects of Topical Kiwifruit on Healing of Chronic Bedsore

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Abstract Kiwifruit (*Actindia deliciosa*) is demonstrated to have antibacterial and pro-angiogenic effect. Moreover, this fruit contains proteolytic enzymes (actinidin) and ascorbic acid. Considering these properties and based on the results of recent animal studies, we carried out this study to evaluate the effects of kiwifruit on bedsore in clinical settings. Forty patients with stage 2–3 sacral bedsore, preferably paraplegic, quadriplegic, and/or hemiplegic, were allocated into two groups of experiment and control. Under local anesthesia and sedation, ulcers of the experiment and control groups were dressed with pure extract of kiwifruit and normal saline, respectively, on a daily basis for 21 days. The ulcers were examined and photographed weekly. Pre- and postintervention biopsies were taken from the ulcers to perform microbiological and histological study. Mean reduction in surface area of bedsore in the experiment group was significantly higher than the control group (486.47 vs. 117.38 mm, $p < 0.001$). The amount of collagen and granulation tissue were significantly higher in experiment groups than the control group (p value 0.005 and 0.02, respectively). Significantly higher levels of angiogenesis and vascularization were found in the kiwifruit-treated patients ($p < 0.02$). In addition, obvious antibacterial effect was observed in the kiwifruit group. Natural compounds in the kiwifruit, including protein-dissolving enzymes (actinidin) and antibacterial agents, improve different aspects of the wound healing process. Based on its benefits and safety, we conclude that using kiwifruit is a simple, applicable, and effective way for treatment of bedsore.

Keywords Kiwifruit · Bedsore · Wound healing

Introduction

Pressure ulcer is a pretty debilitating and common problem that affects disabled elderly patients. The incidence varies in different institutions; for instance, recent studies on bedridden patients estimated it to be 3.9–7.1 % in hospitalized patients, 4.3–13.9 % in nursing home residents [1–4], and up to 39 % in those with spinal cord injuries [5]. Patients of intensive care units have the highest rate of this sort of ulcer [4]. Pressure ulcers can result in enormous expenditures for patients, as well as for medical centers, and also produce pain, loss of economic productivity, significant infirmity, and high mortality rate [6, 7].

Prompt identification and intervention are fundamental for successful treatment of chronic wounds. The focus of wound bed preparation should be on providing a moist environment, in addition to accelerated granulation tissue formation, angiogenesis, and reduced bacterial load in the ulcer.

More than 80 % of the world's population rely on traditional medicine including plant-based products for treatment of various skin problems, especially wound infections and ulcers [8]. The explanation of the concept of topical medicinal herbs is ascribed to Avicenna, the Persian physician and scholar (980–1037 AD) [9].

It is currently accepted that kiwifruit contains potent protein-dissolving enzymes (actinidin) and antibacterial agents that could play an important role in wound healing process. Based on several in vitro and animal studies, the kiwifruit has proven effects in ulcer debridement, angiogenesis, and disinfection; moreover, it has dramatic effects on healing process of burn wounds [9, 10]. Given the above,

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Table 1 Macroscopic and microscopic changes

	Case		Control		<i>p</i> value
	Day 0	Day 21	Day 0	Day 21	
Wound Surface (mm ²) ^a	866.24±181.18	379.77±93.50	737.58±139.94	620.19±121.36	<0.0001
Epithelialization ^b	0.72	0.72	0	0	1
Vascularization ^b	0.22	1.8	0	0.75	0.001
Collagen formation ^b	0.42	2.1	0.33	0.60	<0.0001
Inflammation ^b	2.27	2.11	1.75	0.92	0.001
Granulation ^b	0.11	1.83	0	0.50	0.001
Percentage positive wound culture ^c	72 %	44 %	83 %	67 %	0.17

^aData presented as mean ± SD^bData presented as mean rank^cData presented as percentage

this study was purposed to investigate the effectiveness of fresh kiwifruit dressing on treatment of pressure ulcers.

Materials and Methods

In a randomized clinical trial study, by maintaining the respective rules of research ethical and investigative committee of the hospital, 40 patients with pressure ulcer at stages 2 or 3 (Table 1) were divided randomly in two groups (groups K and C). Patients of neither group had obvious finding of underlying osteomyelitis, radiologically and clinically. Routine low-pressure air mattress was used for all bed-bound patients. Albumin levels were taken to ensure proper nutrition in each case. At first, mandatory wound bed preparation such as removal of nonviable tissue and drainage of abscess was done for patients who need emergent intervention. The wounds were anesthetized by local lidocaine 1 %, accompanied by sedation with ketamine hydrochloride under sterile condition, and the first specimen from wound place for primary culture and histological studies was taken, upon arrival, to determine initial size of the wound. All samples were photographed. Wound of all patients were kept in environment of the hospital under study and had sterile dressing.

Twenty-four hours later, wounds were irrigated with sterile normal saline in all groups. The ulcers were covered with

prepared kiwifruit, in group K. Pure extract of fresh kiwifruit after being completely mashed by a mixer was poured in gavage syringe of 50 cc at bedside, and it was placed on the whole surface of the wound with 3-mm thickness. In group C, the wounds were dressed with Vaseline sterile gauze without using any additional agents. In both groups, ulcers were covered with sterile gauze, which were affixed to skin with Omnifix (Braun, Melsungen, Germany), a latex-free, nonwoven retention tape. Maintaining sterility, dressings were changed twice daily in both groups following irrigation with sterile normal saline. Macroscopically, wound evaluation was performed every day with digital camera for up to 3 weeks. In day 21, wound biopsy and culture were obtained under sterile condition following administration of local anesthesia to the wounds to be sent after photography for culturing and histopathology was performed. The surface of the ulcers was measured on the grid-scored digital photos by Sigma Scan PRO® version 5.0 computer software.

The specimens were stained with hematoxylin and eosin (H&E), Masson (collagen marker), and CD31 immunohistochemistry (IHC) marker, and one pathologist who is blinded to the experiment groups accomplished pathological investigation under Olympus optical microscope. In terms of pathological survey, parameters such as epithelialization, inflammation, granulation, collagen synthesis, and vascularization (angiogenesis) were investigated with the following

Fig. 1 Progress of wound healing in a patient treated with kiwifruit

Fig. 2 Histopathology sample of a patient treated with kiwifruit. **a** Section showing low density of inflammatory cell in the dermis and increased collagen bundles (H&E). **b** Moderate-density vascular

formation in dermis (IHC staining with CD31). **c** Moderate collagen bundle deposition in the dermis (Masson trichrome staining)

scoring system: 0, none; 1, minimal; 2, mild; 3, moderate; and 4, maximum.

Streptococcus, *Staphylococcus aureus*, *Staphylococcus* coagulase negative, and *Pseudomonas aeruginosa* were the organisms investigated in the cultures that were taken from the ulcers. The data of all groups were evaluated by SPSS software V.16. All data were analyzed by the Kruskal–Wallis test, Mann–Whitney test, and Chi-square tests. A $p < 0.05$ was considered as statistically significant.

Results

Forty patients with pressure ulcers were enrolled in a randomized clinical study. Macroscopic and microscopic changes are summarized in Table 1. Significant wound healing activity was observed in patients treated with the kiwifruit compared with those who received the reference standard treatments.

Macroscopic Findings

1. *Wound area*: Applying kiwifruit extract significantly accelerated scar detachment in the experiment group. The scars detached spontaneously from the wound beds in B2 group patients later than day 21, whereas this happened before day 21 in the experiment group.

Fig. 3 Histopathology sample of a patient of the control group. **a** Section showing loose dermis collagen bundle associated with inflammatory cells (Masson trichrome staining). **b** Low density of vascular structure (IHC staining with CD31)

Measurement of wound area showed significant reduction in wound size of group B1 as compared with that of group B2 in the first and 21st days of the experiment ($p < 0.006$) (Fig. 1).

2. *Down stage of the wound*: Evaluation of wound stage showed significant reduction in group B1 as compared with B2 in the first and 21st days of the experiment ($p < 0.049$).
3. *Macroscopic hyperemia and edema*: In group B1, macroscopic hyperemia and edema levels were higher on days 3 and 5 in comparison to the corresponding control groups. However, between days 11 and 20, the level was significantly lower than that of the control group ($p < 0.05$).

Microscopic Findings

The results of histological scoring of the patients at the end of the third week and its comparison with the values at the beginning of the experiment are shown in Table 1, and the histopathological samples are presented in Figs. 2 and 3.

1. *Epithelialization*: Because most patients with bedsore had stages 2 and 3 lesions, even after 21 days, only 16.3 % of patients with stage 2 bedsore recovered to stage 1, and epithelialization was observed ($p < 0.3$).

2. *Granulation score*: The granulation score was higher in groups B1 compared with group B2, and the difference was statistically significant ($p < 0.02$).
3. *Inflammation score*: In group B1, the number of inflammatory cells was lower than that in group B2, but the difference was not statistically significant ($p < 1$).
4. *Collagen formation*: The amount of collagen in group B1 was found to be significantly more than that in group B2 ($p < 0.005$).
5. *Angiogenesis*: Vascularization score in group B1 was found to be significantly higher than that in group B2 ($p < 0.02$).

Microbiological Findings

Significant antibacterial activity was observed in patient treated with the kiwifruit (B1) compared with control group (B2). The difference was statistically significant ($p < 0.001$).

Microscopic evaluation of wounds for blood vessel count and wound-base collagen deposition revealed significant difference between the two groups. The number of patient with ischemic ulcers (such as those with Burger's disease) was not enough for statistical evaluation. Nevertheless, it was observed that, compared with the experiment group, scar tissue in these patients required a longer time for autolysis detachment.

Discussion

The history of using herbal dissolving enzymes for chemical wound debridement dates back to World War II [11]. Scientists try to investigate the effectiveness of herbal products, which have been used in Asia and Africa for centuries, in the treatment of different types of wound [12]. Pressure wound is one of these sorts of wound. Bedsore is a common, costly, and debilitating type of wound that usually afflicts people with advanced age, physical or cognitive disability, or multiple health problems [13]. Based on the suggested safety and efficacy for application of kiwifruit wound dressing in previous animal study [14], we investigated this method on human cases with bedsore and found it a useful method. Previous studies have reported various clinical effects for kiwifruit, such as debridement of dead tissue and antibacterial effect [10, 15].

This was confirmed in our study: kiwifruit extract accelerated scar detachment significantly. This effect may be attributed to some ingredients of kiwifruit including ascorbic acid that works as an scavenger, and a strong protein-dissolving enzyme called *actinidin* [10, 15]. Actinidin is one kind of cysteine proteases (CPs) found in kiwifruit, which is responsible for the well known proteolytic and meat-tenderizing effect of kiwi [14, 16]. These substances make kiwifruit a good option for herbal debridement.

Supporting previous studies, in this study, kiwifruit showed significant antibacterial properties [10, 14]. It may be related to the composing ingredients of kiwifruit. High concentration of CPs in many fruits such as kiwi is believed to have antibacterial, antifungal, and even anti-insect role [10, 16]. In vitro studies reported the antibacterial activity of 18 fractions of kiwifruit extracts against gram-positive and gram-negative bacteria, and fungi [10, 17]. Because wound infection is a common problem in patients with bedsore, especially those with fecal incontinence, kiwifruit dressing can be helpful regarding infection control.

Better vascularization, found in pressure wounds dressed by kiwifruit, is similar to animal findings [14]. Although angiogenic compounds are found in several plants such as *Aloe vera*, they have not been reported in kiwifruit [18]. Hence, it is thought that kiwifruit may be rich in some sorts of angiogenesis modulators that are essential for the healing process [14].

In addition to macroscopic improvement, histologic evaluation of wounds showed that kiwifruit dressing significantly increases granulation score and collagen formation. Given these positive effects, it is not surprising to find significantly reduced wound surface, as well as improved wound sage, in kiwifruit-treated bedsore.

A major concern in the treatment with herbal medications is unknown side effects including allergic reactions. Fortunately, similar to the previous experience on rats [14], no significant anaphylactic reaction was seen in patients treated with kiwifruit.

In light of the useful characteristics of kiwifruit including debridement of devitalized tissue—without detrimental effects on the healing process—angiogenesis, and antibacterial effect, we can conclude that this method is a simple, applicable, and effective way for the treatment of bedsore.

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