



Omega Fatty Acid-Based Therapy for Healing of Recalcitrant Wounds in Patients with Complex Comorbidities

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ABSTRACT

The human body possesses the unique ability to repair itself after injury through complex, sequential phases. Current development of advanced wound care therapies generally focuses on addressing a single aspect of this biological process that can result in delayed or ineffective wound healing. When patients present with further systemic and local confounding pathologies, it can result in painful, chronic wounds that are especially challenging to treat.

In this case report, the authors demonstrate how treatment with a novel multimodal wound matrix expedited healing and decreased pain in two patients who had each been unresponsive to treatment with advanced modalities for more than 7 months. The first patient had factor V Leiden, and the second patient had sickle cell disease. Use of a once-weekly treatment protocol with the multimodal wound matrix, combined with sharp debridement when deemed clinically necessary, resulted in elimination of pain and expedited wound healing to closure. The wound matrix's omega fatty acid-based formulation is designed to target multiple factors common among hard-to-heal wounds that when not addressed can adversely inhibit the wound-healing cascade.

KEYWORDS: collagen, factor V, fatty acids, omega fatty acid, sickle cell anemia, skin care, venous ulcer

ADV SKIN WOUND CARE 2024;37:550-4.

DOI: 10.1097/ASW.0000000000000207

INTRODUCTION

The human body is an engineering marvel, whose functions include the ability to repair itself after injury.¹ Chronic wounds are defined as those that fail to progress through this normal process of healing. Advanced modalities for the management of chronic wounds, such as skin substitutes, have a significant presence in the specialty of wound care.² Benefits of these technologies are well documented, with ever-growing data further supporting the efficacy of products in this category.² However, as research provides a greater understanding of the interactive processes involved in wound healing, a striking disconnect has become apparent between what providers understand as the traditional approach to chronic wound management versus how the body proceeds with healing.

The wound care community has long held that no two wounds are alike, even when they exist on the same individual. However, product development for expedited healing has focused on creating advanced wound care therapies that address only a single aspect or phase of wound healing, such as assistance with debridement for removal of nonviable tissue and biofilm, providing a temporary scaffold for cellular migration,^{3,4} or the addition of growth factors to promote angiogenesis and epithelialization.⁵ Wound management in this fashion typically requires wound care specialists to use multiple products over the course of treatment, significantly increasing treatment cost.⁶ As such, it is not surprising that the efficacy of treatment with skin substitutes is affected by factors beyond the skin substitute itself, including any products used in conjunction (eg, to prepare the wound bed).²

Understanding the interactive processes involved in wound healing and providing the patient with the necessary elements to assist the body through this cascade of physiologic events are fundamental to achieving wound resolution in a timely and orderly manner. A healthy body

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does not generally develop chronic wounds: chronic wounds develop when the body is missing the necessary components for the natural function of healing to occur. This central concept and clinical perspective states that when the wound receives the key components needed throughout wound healing, wound resolution is possible. This represents “personalized wound healing,” with delivery of the components required to support each phase of the physiologic healing cascade.

This concept of personalized wound healing led to the development of Omeza Complete Matrix (OCM; Omeza, LLC), a biocompatible wound matrix composed primarily of naturally occurring components, including cod liver oil, (the primary source of the omega-3s), cold-water fish peptides, other plant-based oils and waxes, and vitamins and nutrients to facilitate biofilm reduction and enhance cell proliferation and healing.⁷ The product is designed to create an anhydrous conformable sheet that serves as a matrix for cellular infiltration for tissue regeneration. It is applied to the wound as a solid and then “melts” into the wound as it warms to body temperature. The combination of optimal medical management with the use of the multimodal wound matrix to function throughout all phases of wound healing is intended to reduce inflammation, prevent bacterial ingress, maintain moisture, and enhance local wound perfusion.

In this case report, the authors demonstrate how the use of this novel multimodal wound matrix expedited healing and decreased pain in two patients with systemic and local factors that had resulted in painful, chronic, nonhealing wounds of greater than 7 months’ duration that were previously unresponsive to current modalities. Each patient provided written informed consent to publish the case details and associated images.

CASE 1

A 54-year-old African American man presented to the ED with a 1-month history of a nonhealing ulcer on the medial aspect of his left leg. He reported self-treating the area. His chief concerns were pain and odor associated with the ulceration. The patient reported a medical history of hypertension and a medical and family history of factor V Leiden and deep venous thrombosis. He also reported a surgical history of paraumbilical hernia repair and inferior vena cava filter placement. The patient reported taking amlodipine, hydrochlorothiazide, and warfarin and denied any known drug allergies. The patient endorsed smoking a half-pack of cigarettes per day for 30 years and denied alcohol and drug use.

A focused examination of the left leg revealed a full-thickness ulceration on the distal medial aspect measuring approximately 12.0 × 6.0 cm with a mixed granular and fibrotic base; areas of necrosis were noted in the posterior distal aspect of the wound (Figure 1A). The ED

physician diagnosed the patient with a venous leg ulceration. The patient was subsequently admitted for medical and surgical management. The patient underwent surgical intervention consisting of hydrosurgical debridement and application of an acellular fish-skin graft while hospitalized. The patient was discharged home with an outpatient management plan of weekly clinic visits consisting of wound evaluation; debridement, when deemed clinically necessary; and compression therapy.

The wound failed to show progression toward resolution after 6 months of outpatient management (Figure 1B). The patient also complained of pain associated with the wound that he rated as 10/10 on the visual analog pain scale and required the use of narcotic analgesics. His physicians decided to initiate once-weekly use of the multimodal wound matrix. The treatment protocol included a 5- to 10-minute wound preparation with an anhydrous periwound preparation followed by wound debridement. The physician then applied the wound matrix to the wound bed to support tissue regeneration. Finally, an anhydrous skin protectant was applied to the periwound skin from knees to toes in preparation for application of a secondary dressing (Figure 1C). The wound was covered with a nonadherent petrolatum-based gauze and mild compression in the form of a multilayer wrap.

Use of this weekly treatment protocol, with wound debridement performed when deemed clinically necessary, resulted in rapid pain resolution, negating the need for narcotic analgesics (Figure 1D, E). Wound resolution was achieved with 100% reepithelialization at 11 weeks, after 9 months’ total duration, including 6 months of previously failed therapy (Figure 1F).

CASE 2

A 31-year-old woman with a medical history of sickle cell disease presented to the ED with a draining wound on her right ankle that had been present for 7 months (Figure 2A). The patient reported pain associated with the wound rated as 10/10 on the visual analog pain scale and that she was unable to walk, put on shoes, or sleep and that wound care was “a nightmare” because the pain was unbearable. Other pertinent medical and surgical history included an ectopic pregnancy with salpingectomy and a cholecystectomy. The patient reported her current medications to include hydroxyurea, oxycodone/acetaminophen, folic acid, and an albuterol inhaler. She reported an allergy to morphine. The patient endorsed smoking a half-pack of cigarettes a day for 14 years and social marijuana use.

Focused examination of her right leg revealed an approximately 5.0 × 5.0-cm full-thickness ulceration on the lateral aspect of the ankle with a mixed fibrotic and necrotic tissue base. Hyperpigmentation extended approximately 2.0 cm from the edge of the wound bed on the periwound skin. A second full-thickness ulceration

Figure 1. CASE 1 WOUND HEALING PROGRESS

Clinical appearance of the wound (A) prior to initial surgical debridement; (B) after outpatient management before treatment with the wound matrix; (C) following application of the multimodal wound matrix; (D) after 4 weeks of weekly treatment; and (E) after 6 weeks of weekly treatment. F, Wound resolution at 11 weeks.



measuring approximately 2.0×1.0 cm with a mixed fibrotic and necrotic base was located posterior to the larger ulceration with an approximately 1.0-cm-wide area of closed skin between the two ulcerations (Figure 2A).

The patient was diagnosed with sepsis secondary to her lower leg ulceration and active sickle cell crisis. The patient underwent surgical intervention consisting of hydrosurgical debridement and application of an acellular fish-skin graft while hospitalized and blood transfusions for treatment of her sickle cell crisis. The patient was discharged with an outpatient management plan of weekly clinic visits consisting of wound evaluation, debridement when deemed clinically necessary, and compression therapy.

The wound failed to show progression toward resolution after 2 months of outpatient management (Figure 2B, C). The attending physician and residents decided to initiate weekly use of the multimodal wound matrix. The treatment protocol included a 5- to 10-minute preparation of the periwound skin with an anhydrous periwound formulation and application of the wound matrix to the wound bed to support tissue regeneration (Figure 2D). An anhydrous skin protectant was then applied to the skin from knee to toes in preparation for application of a secondary dressing. The wound bed was covered with a nonadherent petrolatum gauze, and a compressive dressing was applied to the lower leg.

Figure 2. CASE 2 WOUND HEALING PROGRESS

Clinical appearance of the wound (A) at the time of initial presentation; (B) after outpatient management; (C) with application of the multimodal wound matrix; (D) after 2 weeks of weekly treatment with the wound matrix; and (E) after 4 weeks of weekly treatment. F, Wound resolution at 7 weeks.



This protocol was performed once per week for 7 weeks. Sharp debridement was deemed necessary during one of these weekly visits. Use of this treatment protocol resulted in rapid pain resolution, negating the need for narcotic analgesics (Figure 2E). The patient reported improvement in her mental health and quality of life and reduced pain with ambulation. Wound resolution was achieved at 7 weeks with treatment of the wound matrix, after nearly 11 months' duration, including 2 months of previously failed advanced wound therapy (Figure 2F).

DISCUSSION

The two cases presented here demonstrate the ability of this multimodal wound matrix to expedite healing and eliminate pain in patients with systemic and local factors that resulted in painful, chronic, nonhealing wounds. Both patients showed substantial clinical improvement and full healing after having been previously unresponsive to current modalities, which included skin substitutes.

In addition to being stalled in a dysfunctional inflammatory phase of healing, the presence of constant pain can hinder quality of life and impede wound healing.⁸ In case 1, the wound failed to progress toward healing despite surgical debridement and application of a skin substitute. Use of the wound matrix formulation was initiated after 6 months of prior treatment and subsequently expedited healing and eliminated the patient's pain. The same treatment protocol also resulted in wound resolution and elimination of pain in the patient in case 2, who also had not improved after 9 months of prior advanced wound care treatment. Despite established inhibitory effects on wound healing of hydroxyurea (prescribed to lessen the effects of sickle cell disease), albuterol (a steroid prescribed for asthma), and nicotine, the debilitating wounds of this patient with sickle cell disease resolved in 6 weeks with further remodeling noted at week 8 of treatment with the wound matrix.

Enhancing reparative processes by providing the components needed locally by the wound promotes healing.

A comprehensive approach to wound healing acknowledges the inherent limitations of the patient and provides support for all aspects of the physiologic series of events that is needed for tissue repair and regeneration.

The product used in these two cases was developed and formulated to enhance the patient's own healing mechanisms and to combat three major local wound factors associated with delayed healing: bioburden/biofilm production,⁹ inflammation,⁹ and hypoxia/lack of perfusion.¹⁰ The wound matrix was designed as an amorphous solid to rapidly transform into a conformable, malleable sheet when applied directly to the wound, enabling it to fill soft tissue cavities, areas of undermining, and wound tunnels.

The formulation contains nutrients necessary to support wound healing through tissue regeneration, cellular proliferation, and cell migration. Omega-3 polyunsaturated fatty acids have been shown to inhibit bacterial growth and biofilm formation.^{11,12} *Staphylococcus aureus*, including multidrug-resistant *S aureus*, *Staphylococcus epidermidis*, and *Pseudomonas aeruginosa* planktonic cell growth, and biofilm formation are inhibited by high concentrations of two major omega-3 polyunsaturated fatty acids, docosahexaenoic acid and eicosapentaenoic acid.^{11,12} Omega fatty acids may also assist with the transition of a wound from a stalled, dysfunctional inflammatory phase of healing to the proliferative phase of wound healing, hallmarked by angiogenesis.¹ In preclinical trials, omega-3 polyunsaturated fatty acid reduced inflammatory cell recruitment,^{13,14} enhanced angiogenesis in the deep layers of dermis,¹⁵ and promoted recruitment of fibroblasts resulting in accelerated wound closure.¹³⁻¹⁶

Limitations

The primary limitations of this case report are the small sample size and limited research on the optimal application method and concentration of the collagen matrix for use in wound healing.¹⁴ Despite the small sample size, the cases presented here are representative examples of patients seen for the treatment of chronic wounds, with multiple systemic and local factors that impede the body's normal wound-healing function. Although both patients received advanced wound care by specialized wound care providers, wound healing was not obtained until the patients' respective underlying conditions were addressed and the multimodal wound matrix product was implemented.

Further randomized trials and controlled studies are being conducted to determine, among other aspects, the performance of the wound matrix in larger cohorts and in other hard-to-heal wound types. These trials will also identify the optimal concentration/dose of the wound matrix.

CONCLUSIONS

Wound healing in patients with chronic, nonhealing wounds is often compromised by a multitude of systemic and local wound factors associated with delayed healing. Treatment of these patients should combine medical, lifestyle, and psychosocial optimization with the use of wound care treatment products that mitigate the negative local wound factors hindering healing.

In the two complex cases presented here, both patients had shown an inability to heal for at least 7 months and were unresponsive to available advanced treatments. They are representative of patients seen daily for chronic wound care management and those with multiple, often disabling, systemic and local factors that can adversely affect wound healing. Although neither patient had responded previously to advanced wound care modalities, treatment with the multimodal wound matrix, which was designed to reduce bioburden and inflammation and enhance local tissue perfusion, resulted in both patients experiencing wound healing and the elimination of pain. ●

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