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Activated, Type I Collagen (CellerateRx) and Its Effectiveness in Healing Recalcitrant Diabetic Wounds: A Case Presentation

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and Kimberly Swartz**

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Activated, Type I Collagen (CellerateRx) and Its Effectiveness in Healing Recalcitrant Diabetic Wounds: A Case Presentation

Martin I. Newman, MD, FACS; Larry G. Baratta, MD, PhD; and Kimberly Swartz

ABSTRACT

OBJECTIVE: To review the authors' experience with activated type I collagen in the treatment of recalcitrant wounds in the diabetic population resulting from minor trauma and/or venous stasis disease. With regard to activated collagen, CellerateRx's patented activated collagen fragments are a fraction of the size of the native collagen molecules and particles found in other products, delivering the benefits of collagen to the body immediately.

DESIGN: A 2-case presentation wherein patients were treated with CellerateRx (activated, fragmented, and nonintact type I collagen) in a gel and powder form.

SUBJECTS: Two middle-aged diabetic male patients with lower extremity wounds refractory to conservative wound care.

RESULTS: Complete resolution of recalcitrant wounds in 6 to 7 weeks.

CONCLUSIONS: Wound resolution was evident when using the authors' practice protocol, which includes the application of activated collagen. The inherent properties of type I collagen may contribute to a more rapid healing process.

by the US Food and Drug Administration to treat diabetic and nondiabetic wounds, Stages II-IV pressure ulcers, ulcers resulting from venous stasis and arterial insufficiency, traumatic wounds, and superficial and surgical wounds, including superficial and partial-thickness burns (excluding full-thickness burns). The collagen molecules found in this product are 1/100th of the size of naturally occurring collagen and present more surface area. Thus, the patient can benefit from the collagen more quickly.

Collagen has been identified as having multiple functions in the healing process. Primarily, collagen possesses the following properties. (1) *Hemostasis*: collagen binds to fibronectin,^{1,2} causing platelet adhesion and aggregation.³ (2) *Autolysis*: it has the propensity to chemotactically attract monocytes and leukocytes.^{4,5} (3) *Angiogenesis*: collagen attracts monocytes,^{4,5} which transform into macrophages.⁶ These macrophages release substances that result in fibroplasia and angiogenesis.⁷ Collagen provides support for the growth of new capillaries.^{7,8} The presence of new capillaries is essential for the deposition of new fibers.⁷ (4) *Fibroblast activity*: collagen binds with fibronectin,^{1,2} which promotes cell binding.^{9,10} Collagen is chemotactic to fibroblasts,¹¹ which govern the restoration of new tissue¹² by depositing oriented and organized fibers.^{13,14} (5) *Reepithelialization*: collagen directly supports the growth,^{15,16} attachment,¹⁷ differentiation,^{16,17} and migration¹⁸ of keratinocytes.

INTRODUCTION

Two middle-aged men presented with diabetic wounds to the lower extremities arising from minor incidental trauma and/or venous stasis disease; the wounds were chronic in nature and refractory to standard treatment. This short case study aims to examine the use of fragmented, activated, type I collagen in treating these wounds. The authors have used this short case study to stimulate a larger, currently ongoing study. The collagen provided and used in the treatment of these patients was in the powder-and-gel form of CellerateRx (Wound Care Innovations, LLC, Fort Lauderdale, Florida) and was provided by the manufacturer, The Hymed Group. CellerateRx is cleared

METHODS

An examination was performed on 2 patients selected for evaluation based on the diagnosis of recalcitrant diabetic wounds and treatment that included collagen therapy in the form of CellerateRx. There were no exclusion criteria. In this process, charts, wound measurements, and photographs were reviewed. The following criteria were examined: granulation tissue formation, time to form, and quality of the new tissue; ability to achieve epithelialization; patient comfort and tolerance to the dressing; and ability to stop bleeding, if applicable.

Case Report

Figure 1.

JUNE 28, 2005

Measurement: $4.0 \times 2.3 \times 0.1$ cm.



In the authors' clinical practice, CellerateRx is applied as part of a protocol that includes a program of strict elevation; Unna boot wrapping with frequent changes; and the application of CellerateRx in the form of a paste composed of both gel and powder.

Elevation is recommended to the authors' patients with lower extremity wounds for which it is not contraindicated. The authors' usually recommend a protocol of "elevation of the involved extremity, above the level of the heart, 4 times a day, for 20 minutes each time." Again, unless contraindicated, we also ask patients to "elevate the involved extremity during sleep hours on pillows."

Unna boots are used on patients with no medical or other contraindications. In the authors' practice, the Unna-Flex (ConvaTec, Princeton, New Jersey) is used. The boots are

Figure 2.

JULY 19, 2005

Flattening and advancement of wound edges noted. On July 26, 2005, the wound measurements were $4.0 \times 3.0 \times 0.5$ cm. No maceration, no erythema evident.



Figure 3.

JULY 29, 2005

Measurement: $3.8 \times 2.7 \times 0.2$ cm. No maceration, no erythema evident. On August 12, 2005, the wound measurements were recorded as $4.0 \times 2.5 \times 0.2$ cm. No maceration and no erythema evident.



changed twice weekly and wrapped with a single layer of 4" Coban (3M Medical Division, St Paul, Minnesota). Every 2 to 3 weeks, the boots are removed for a 48-hour period. This helps provide the patient with some relief from the effort associated with this form of dressing.

At each biweekly dressing change, activated type I collagen is applied to the wound in the form of CellerateRx paste. The paste is compounded at the time of the dressing change in the following process:

- On a sterile surface, 2 mL of CellerateRx gel (quantity adjusted to wound size) is dispensed. CellerateRx powder is sprinkled on the gel surface sufficient in amount to completely cover the gel.

Figure 4.

AUGUST 19, 2005

Measurement: $2.3 \times 1.9 \times 0.2$ cm. No maceration, no erythema evident. Hemoglobin level was 6.7 g/dL.

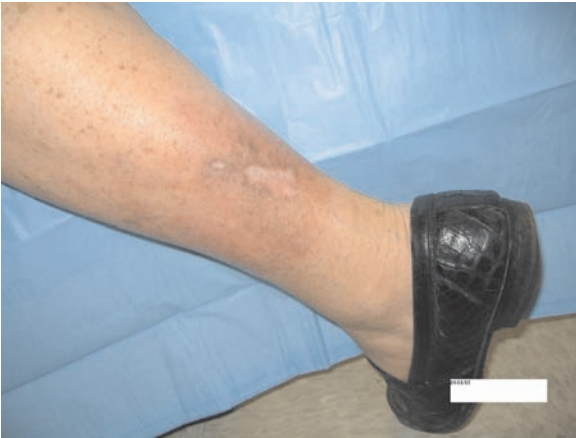


Case Report

Figure 5.

SEPTEMBER 1, 2005

Wound resolution demonstrating minimal scarring.



- The wooden end of a sterile cotton-tip applicator is used to mix the powder and gel into a paste.
- The Unna boot application is begun at the metatarsal phalangeal joint and wrapped on the lower extremity until the wound is encountered. The CellerateRx paste is then applied, and the wrap is continued to completion. An outer wrap has been applied.
- At subsequent dressing changes the CellerateRx powder-and-gel mixture is reapplied.
- No surgical debridement is conducted between dressing changes.
- Patients are instructed to keep the dressing clean and dry between changes and to elevate the involved extremity according to our protocol as outlined above.

Figure 6.

MAY 3, 2005

Measurement: 2.0 × 3.0 × 1.0 cm. With moderate exudation and no maceration or erythema evident.

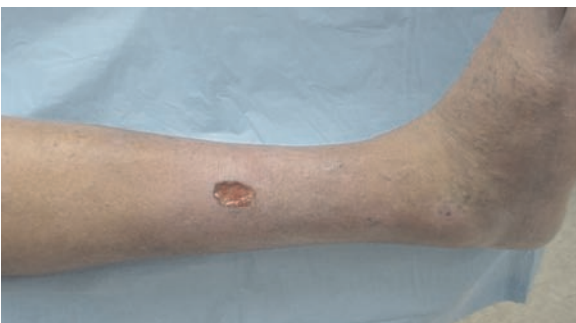


Figure 7.

JUNE 21, 2005

Measurement: 1.0 × 2.0 × 0.2 cm. No maceration and no erythema evident.



RESULTS FOR PATIENT 1

Patient History

A 75-year-old man presented with a cellulitic lesion on the lower left ankle. A history of asthma, morbid obesity, psoriasis, hypertension, and arthritis was noted. The patient had experienced a shingles outbreak on his trunk a few weeks before seeking consultation to this clinic. Subsequently, he noticed a wound developed on his left ankle that was self-treated. His current medication included fluticasone propionate/salmeterol (Advair), montelukast (Singulair), amlodipine besylate (Norvasc), aspirin, and naproxen. The patient was a nonsmoker and did not consume alcohol. He had no known allergies.

Wound and Physical Examination

Examination of the wound revealed a 5.0 × 7.0-cm cellulitic lesion with mild granulation on the posterior aspect of the lower left ankle, which was malodorous with greenish

Figure 8.

JUNE 24, 2005

Measurement: 1.0 × 1.5 cm. No maceration and no erythema evident.



Case Report

discharge. The wound clinically appeared to be *Pseudomonas* and was not cultured. This diagnosis resulted in a course of ciprofloxacin, which aided in the healing. Bilateral edema was present with 2+ pulses on the left assessed. Initial treatment plan was an application of silver sulfadiazine (Silvadene) and standard secondary dressings. The patient was noncompliant with this treatment plan over the course of 3 months, and his clinic visits were infrequent.

Clinical Course and Treatment History

On June 21, 2005, the patient's wound appeared as a granular base and measured 2.5 × 4.5 cm. Treatment with CellerateRx powder and gel, which was wrapped in an Unna boot, was initiated. The patient returned to the clinic on June 28, 2005 (Figure 1), and informed clinicians that his primary care physician had diagnosed him with diabetes. He had begun a regimen of insulin therapy and oral hypoglycemics. The patient informed us that on June 8, 2005, a blood glucose finger-stick test was 245 g/dL, and hemoglobin A1c level was 12.3 mg/dL. The use of insulin therapy was seen to effectively control his blood glucose and subsequently positively affected the healing of his wound. Although this cannot be overlooked, the authors do not consider it the only factor to facilitate his healing. Over the course of the documented wound care, different observers measured the wound.

Conclusion

In 7 weeks, the patient's wound resolved using CellerateRx powder-and-gel combination (Figures 1–5).

RESULTS FOR PATIENT 2

Patient History

A 62-year-old man presented with a nonhealing wound of 1-month duration. The patient has had type 1 diabetes for more than 20 years. He also had a history of venous stasis disease, gluten enteropathy, bilateral lower extremity diabetic neuropathy, hypercholesterolemia, spinal stenosis, and chronic back pain. His current medication included gabapentin (Neurontin), lovastatin, insulin pump, and over-the-counter nonsteroidal anti-inflammatory agents. He had no known allergies and did not smoke or drink alcohol. The patient has a history of self-resolving wounds on the feet and legs that usually resolve after treatment using a home remedy of hydrogen peroxide and triple antibiotic solution.

Wound and Physical Examination

Initial physical examination revealed a wound located on the anterior lateral aspect of the right lower extremity measuring 1.4 × 2.0 cm, chronic in appearance, well granulated, and

with no erythema and no apparent infection. The surrounding skin presented with the stigmata of chronic venous stasis disease. The skin appeared brawny bilaterally and pigmented at the level of the midcalf. Both ankles had 2+ pitting edema with pulses intact on the left foot and 1+ on the right foot.

Clinical Course and Treatment History

Initial treatment consisted of an Unna boot for 1 week. The patient was noncompliant with both his return visits to the clinic and with following instructions regarding elevating both extremities while at home. Over the course of the following 6 months, the visits to the clinic were sporadic and consisted of wet-to-dry wound dressings.

When the patient returned to the clinic on March 25, 2005, a biopsy was performed of the wound margin, revealing superficial, fragmented crusted skin that is consistent with stasis dermatitis. After a long discussion with the patient about his condition and his noncompliance to medical directives, he agreed to follow consistent, regular wound dressing visits.

Conclusion

In 6 weeks, the patient's wound resolved using CellerateRx powder-and-gel combination (Figures 6–9).

SUMMARY

Factors ranging from poor blood supply¹⁹ to altered macrophage function²⁰ have been implicated in the problematic nature of wounds to the lower extremities. The authors' experience has shown that incorporating CellerateRx powder and/or gel into their practice protocol (either as a primary or adjunctive activated, fragmented, and nonintact collagen preparation) has been a positive one. Compared with the authors' anecdotal, historical experience, these common recalcitrant wounds appear to heal more rapidly and thoroughly with the biweekly application of CellerateRx powder and/or gel after treatment with our multimodality practice regimen. However, the authors do not consider this a scientific study, but a preliminary study to promote a more scientific study with increased control and data collection. This study was intended to stimulate a larger, currently ongoing study.

The authors understand that the wound healing process is a complex issue that has been extensively studied; it is seen to be multifactorial with each element playing a significant role. Based on the positive outcomes using CellerateRx powder and/or gel, the authors will incorporate the product into their wound care protocol. ●

Case Report

Figure 9.

JUNE 28, 2005

Measurement: 0.7 × 1.8 cm. No maceration and no erythema evident.



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