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Clinical Experience with Esterified Hyaluronic Acid Matrix in the Treatment of Chronic Wounds

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Abstract

Introduction: The aim of this study was to evaluate effectiveness of sterified hyaluronic acid matrix (eHAM) for treating chronic wounds. Hyaluronic acid (HA) is an extra cellular polysaccharide found in every human tissue and body fluid. The benefits of using eHAM for chronic wounds still needs to be investigated.

Methods: We are presenting the patients we have treated in our wound care center. Choice of patients was based on clinical grounds where clinic an felt that tissue growth needed to be stimulated and based on availability of the product in clinic and failure of routine treatment modalities. We recorded patient demographics, associated health conditions, wound measurements and characteristics. eHAM was used for full thickness wound safterad quated ebridement and making sure the wound is free of infection. Patients were followed weekly and were corded wound dimensions, pain level, comfort and tolerability. Digital photography was used to document wound progress.

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Results: After 1-3 weeks wounds treated with esterified hyaluronic acids caffold have improved characteristics with healthier vascularized tissue. Patient 1showed very good progress after 2-3 weeks and after that wound stalled. He eventually healed at 8 weeks after second application. Patient 2 showed very good progress over course of 5-6 weeks but she did not heal as she had a large wound and we could not continue this treatment at the time due to product availability. Patient 3 was healed in 4 weeks after single application, after this wound had been refractory prior 3-4 months.

Conclusions: We found esterified hyaluronic acids caffold to be useful in the management of recalcitrant diabetic foot and leg ulcers, venous leg ulcers, and surgical sites wounds. Further studies of large magnitude are needed to better understand clinical applications and indications.

Keywords

Chronic wound; Dermal substitute; Hyaluronic acid

Introduction

HA is an anionic, non-sulfated glycosaminoglycan distributed widely throughout connective, epithelial, and neural tissues. Esterified hyaluronic acid is part of an beneficial dressing that can be used for the treatment of difficult, non-healing wounds, including venous leg ulcers and diabetic foot ulcers. The role of the dermis is essential for the proper orchestration of all phases of the normal wound healing process. Wounds with seriously damaged or even absent dermis consistently show seriously impaired wound healing and/or long-term complications such as hypertrophic scarring. Replacing a damaged dermis requires a dermal matrix that is compatible with, or even stimulates, the process of wound healing [1].

Due to the various cellular interactions of HA, it has a various roles throughout each stage of wound healing [2]. The half-life of HA can present as a challenge because it ranges from less than one to several days, and the turnover of native HA by hyaluronidase is rapid [3]. One method of prolonging the half-life is esterification, which changes the physical properties of HA. HA is esterified to slow down its rapid degradation in wound fluid optimizing the degradation rate for wound healing. eHAM is a dermal matrix comprised of a wound contact layer with an outer barrier layer comprised of a semipermeable silicone membrane. The dermal matrix contact layer is biodegradable, and it acts as a 3-dimensional scaffold for cellular invasion and capillary growth [4].

The aim of this study was to evaluate effectiveness of esterified eHAM for treating chronic wounds. HA is an extracellular polysaccharide found in every human tissue and body fluid. The benefits of using eHAM for chronic wounds still needs to be investigated.

Methods

We are presenting the patients we have treated in our advanced wound care center. Choice of patients was based on clinical grounds where clinician felt that tissue growth needed to be stimulated and based

on availability of the product in clinic and failure of routine treatment modalities. We recorded patient demographics, associated health conditions, wound measurements and characteristics. eHAM was used for full thickness wounds after adequate debridement and making sure the wound is free of infection. Patients were followed weekly and we recorded wound dimensions, pain level, comfort and tolerability. Digital photography was used to document wound progress.

Patient 1:

49 year old African American male with complex past medical history including diabetes mellitus, congestive heart failure episodes and venous hypertension, multiple myeloma on immunosuppressive medicines presented to our wound care center with extensive life and limb threatening ulcers of right leg and foot. (Figure 1) He was treated several months with high dose steroids, antibiotic courses, conservative debridement, topical antiseptic solutions, different dressings and compression wraps. 9 months later he was taken to operating room for split-thickness skin graft. This resulted in partial graft take, reducing significantly wound size, than again stalled. With first eHAM application good improvement is seen in 4 weeks (Figure 2), than again no progress until second application at week 8 (Figure 3), resulting in healed wound at 11 weeks follow up. (Figure 4) Patient was seen again in clinic for a different wound same leg, that healed with 3 weeks of compression wraps. eHAM treated area medial leg had good quality epithelium and no recurrence at 10 months follow up.

Patient 1

Figure 1: Week 0.

Figure 2: Week 4.

Figure 3: Week 8.

Figure 4: Week 11.

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Patient 2:

60 year old African American female with chronic refractory venous ulceration right lateral ankle. Present on/off for 8-10 years. Current continuously opened for about 16 months. (Figure 5) Venous reflux with no intervention options. Underlying osteomyelitis ruled out. She has failed other bioengineered treatments including cellular based. eHAM applied week 0 but did not stay on well due to heavy drainage. eHAM reapplied at week 1, and at week 4 significant improvement was noticed in wound bed quality and 25% decrease in wound size. (Figure 6) Please see attached graph with wound surface illustrating wound progress. Unfortunately we were not able to continue Eham due to availability. Patient strongly refused skin grafting.

Figure 5: Wound was debrided before e HAM application.

Figure 6: 4 weeks later, 25% wound surface decrease and advancing epithelium on edges.

Patient 3:

A 75 year old female with refractory venous ulceration with history of stroke, coronary artery disease, lumbar radiculopathy and impaired mobility. The patient had a wound on her left medial malleol. (Figure 7) We had been treating her for 8 months with compression, debridement and silver type dressings. Initially she had a good response in the first 2-3 months with decrease in size, than wound stalled. After debridment and eHAM application wound was healed in 4 weeks, (Figure 8) and stayed healed at 8 weeks follow up.

Results

After 1-3 weeks wounds treated with esterified hyaluronic acid scaffold have improved characteristics with healthier vascularized tissue. Patient comorbidities are discussed separately for each in next section, but in summary: Patient 1 showed very good progress after 2-3 weeks and after that wound stalled. He eventually healed at 8 weeks after 2-nd application. - Patient 2 showed very good progress over course of 5-6 weeks but she did not heal as she had a large wound and we could not continue this treatment at the time due to product availability. Patient 3 was healed in 4 weeks after single application, after this wound had been refractory prior 3-4 months.

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Figure 7: Wound was debrided before e HAM application.

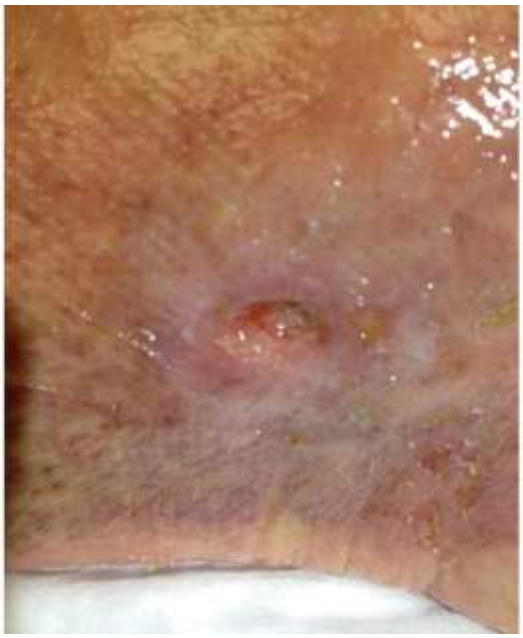

Figure 8: Week 4.

Discussion

HA is an extracellular polysaccharide found in every human tissue and body fluid. Its function depends on its size. Large HA molecules are space filling molecules with regulatory and structural functions, whereas small HA fragments are involved in angiogenesis, inflammation and immunostimulation [5]. HA is known to accumulate in wound tissue and interacts with CD4 inducing pro inflamatory cytokines and

enhances cell infiltration. HA content in fetal wound remains high for larger periods of time than in adults, corresponding with lower hyaluronidase levels, suggesting it may reduce collagen deposbition and scarring [6]. eHAM is a bilaminate construct indicated for full thickness wounds. The outer silicone layer is for mechanical protection and to prevent dessication. The wound contact layer is a nonwoven pad with fibers made of long esterified chains of HA resulting in greater stability than native HA and will postpone degradation. This creates a 3D scaffold that provides support for the colonization by fibroblasts and extracellular matrix (ECM) components, favoring and ordering reconstruction of dermal tissue. This promotes wound healing by facilitating cell migration and dermal repair [7,8]. This scaffold is highly biocompatible [9]. HA is being used in tissue repair such as for chondral and osteochondral lesions due to injury or other pathology [10].

Conclusions

We found esterified hyaluronic acid scaffold to be useful in the management of recalcitrant diabetic foot and leg ulcers, venous leg ulcers, and surgical sites wounds. If wound is not healed at 14-21 days reapplication of the eHAM has beneficial effect and this corresponds to the time frame in which eHAM has been degraded. Further studies of large magnitude are needed to better understand clinical applications and indications.

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