EARLY CLINICAL FINDINGS FROM THE USE OF ENDOFORM™ DERMAL TEMPLATE (*OVINE FORESTOMACH MATRIX*) TO TREAT RECALCITRANT WOUNDS

Brock A. Liden, DPM[1]; Brian R. Ward[2], Barnaby C. H. May PhD[2].
[1]Reynoldsburg Podiatry Centre, 7509 E. Main Street Reynoldsburg, OH 43068, USA.
[2]Mesynthes Limited. P.O. Box 31311, Lower Hutt 5040, New Zealand.

Introduction

There is an urgent need for new technologies to reduce the societal and economic burden of recalcitrant non-healing wounds. These chronic wounds are characterized by a complex etiology that in addition to an underlying medical condition (e.g. diabetes) can also include an imbalance of matrix-metalloproteases, bioburden and bacterial biofilm and an inflammatory response that has failed to resolve. The Endoform™ Dermal Template comprises the biomaterial ovine forestomach matrix (OFM) and is FDA cleared for use in dermal applications, including the treatment of chronic wounds. OFM is a decellularized extracellular matrix that has been shown to retain a native collagen architecture and important ECM-associated secondary molecules, including laminin, fibronectin, glycosaminoglycans and certain growth factors[1]. OFM has been shown to support cell growth and promote cell differentiation and its collagen structure is completely remodelled during the regenerative process[1]. Importantly, in preclinical studies OFM has been shown to promote angiogenesis both in vitro and in in vivo[2]. This current study sought to provide a preliminary evaluation of the Endoform™ Dermal Template in the treatment of difficult to heal wounds.

Methods

This was a non-comparative, open-label evaluation with participants being enrolled as outpatients from the Reynoldsburg Podiatry Clinic (Columbus, OH). Participants presented with a range of lower limb and foot wounds. On first examination, all wounds were surgically debrided down to viable tissue and irrigated with hypochlorous acid solution (Vashe®, PuriCore). Venous ulcers were treated with a silver calcium alginate dressing (Silvercel®, Systagenix) and compression, while diabetic foot ulcers were treated with Santyl® (Healthpoint Biotherapeutics) daily. After the initial seven day qualifying period all wounds were assessed for visible infection (i.e. absence of swelling, pain, purulent drainage, or tracking into the deep tissue planes), and only those wounds that remained free of infection were started on the Endoform™ Dermal Template dressing. Silver calcium alginate dressings and Santyl® treatments were stopped at this time. Using aseptic technique the Endoform™ dressing was trimmed to roughly overlap the wound margins, placed on the wound bed and rehydrated with sterile saline. The color of the dressing changed from white to opaque following rehydration. Light pressure was applied to the dressing to ensure that it conformed to the underlying wound bed. The dressing was covered with a non-adherent secondary dressing (Adaptic®, Systagenix). Compression stockings, exudate control and off-loading were used as required. Participants received weekly follow-up during which time the wound was debrided as required and irrigated to remove loose material. The Endoform™ dressing was reapplied to wounds on a weekly basis and on average each wound received 7 treatments (range 6 to 9 treatments). Changes in the wound granulation tissue, epithelial tissue and wound dimensions were monitored and recorded using digital photography. Following closure, wounds were monitored for a further four weeks.

Results

The Endoform™ dressing was available in a number of size options and both perforated and non-perforated formats. The sizing of the dressings was appropriate for all wounds encountered during the current study. The dressing was robust and easy to handle due to its thickness (approx. 0.25 mm [3]). Once hydrated the dressing conformed well to the underlying wound bed and could be secured with a non-adherent dressing and standard secondary dressings. Even in challenging wounds (e.g. DFUs Participant DB001), the dressing did not shear from the wound bed.

In approximately three days the dressing had adhered strongly to the underlying wound bed presumably due to the infiltration of cells from the periphery. After seven days, the dressing was completely integrated into the wound bed. In some cases only remnants of the dressing remained as an off-white gel that was allowed to remain in place during subsequent applications of Endoform™. We observed an increase in granulation tissue as compared to the amount seen at study enrolment, with a concomitant increase in the vascularity of the wound bed, as assessed by visual inspection. Increases in the presence of granulation tissue were seen after approximately 2-5 weeks of treatment. Pronounced epithelial tissue formation was noted as wounds progressed towards closure. Positive changes were seen across the diverse selection of wound types included in the current study, including wounds that had been stalled in a chronic state for several years (e.g. Participant SC001 and WM001). Several of the wounds had previously failed established surgical interventions (e.g. Dermagraft® and Apligraft®, Participant SC001 and WM001). No adverse effects were reported in any of the participants.

Conclusions

The Endoform™ Dermal Template wound dressing has shown positive clinical outcomes following its use on these five recalcitrant wounds. In each of the described cases there was an improvement in the amount of granulation tissue and epithelialization. All wounds in the study closed following use of the Endoform™ dressing. These promising clinical outcomes support the use of the Endoform™ dressing in the treatment of chronic wounds and further clinical studies are warranted.

References

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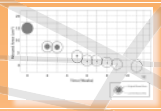
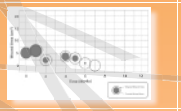
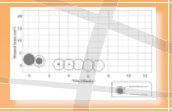
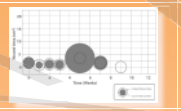
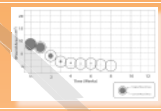
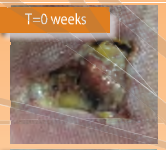
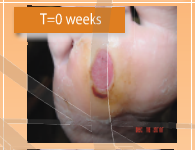
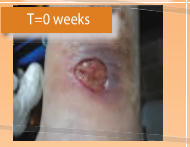
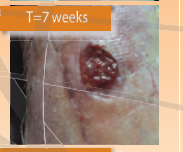
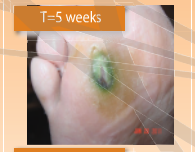
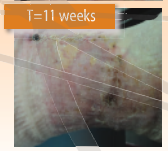
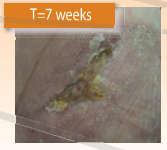
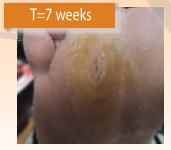
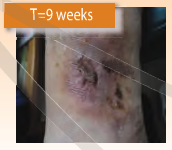
Participant	CB001	CP001	DB001	SC001	WM001
Sex	Female	Male	Male	Female	Male
Co-morbities	• NIDDM • CHF •Edema	• NIDDM • HTN	• Type 1 diabetes • Cellulitis	• Diabetes • Venous reflux • CHF	• HTN
Wound Type	Mixed venous diabetic	Surgical - dehiscence post sub-talar joint fusion and lateral ankle stabilization	Diabetic foot ulcer (type 1)	Mixed venous diabetic	Venous ulcer – dehisced ankle fracture incision
Wound Location	Ankle	Heel	Plantar	Ankle	Ankle
Wound Age	1 year	2 weeks	2 weeks	1+ years	2 years
Initial Wound Size (cm^2)	1 year	2 weeks	2 weeks	1+ years	2 years
Previous Treatments	•Compression •Debridement •Prisma® •Silver collagen •Steroid therapy	•Compression •Santyl® •Debridement (wound edge resection)	•Compression •Debridement •Santyl® •IV Abx (4 weeks)	•Compression •Debridement •Enzymetherapy •Regranex •Dermagraft® (x4) •Prisma®	• Compression •Debridement •Santyl® •Apligraf® (x1) •Dermagraft® (x8) •Matristem® •Biotape® XM
Secondary Dressing	•Adaptic® •Kling®	•Adaptic® •Kling®	•Adaptic® •Kling® •CAM	•Adaptic® •Kling®	•Adaptic® •Kling® •Unna
Outcomes	• Granulation tissue at week 5. • Epithelial tissue at week 4 • Complete healing at week 10. • No re-occurrence	• Granulation tissue at week 3. • Epithelial tissue at week 3 • Complete healing at week 7.	• Granulation tissue at week 2. • Epithelial tissue at week xx • Pseudomonas colonization at week 3. Treated with debridement and VASHE soak. Resumed Endoform™ one week following. • Complete healing in 7 weeks. • No re-occurrence	• Granulation tissue at week 4. • Epithelial tissue at week 4 • Complete healing in 9 weeks.	• Granulation tissue at week 2. • Epithelial tissue at week 3 • Complete healing in 9 weeks. • No re-occurrence
Endoform™ Applications	9	7	6	6	8
Wound Closure Rates					
					
					
					

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