Evaluation of the use of a hyaluronic acid based wound dressing with a silicone fluid transfer dressing

Matthew Livingston RN, CWS
The Honor Health
Scottsdale Osborn Medical Center
Scottsdale, AZ

Debashish Chakravarthy, PhD
Martha Roman, BS
Medline Industries, Inc.
Mundelein, IL

Study # LIT041WC

REFERENCES

1. Wang HJ, et al. Stimulation of skin repair is dependent on fibroblast source and presence of extracellular matrix. *Tissue Eng*. 2004 Jul-Aug;10(7-8):1054-64
2. Adzick NS, Lorenz HP. Cells, matrix, growth factors, and the surgeon. The biology of scarless fetal wound repair. *Ann Surg*. 1994; 220: 10–8.
3. Chen WY, Abatangelo G. Functions of hyaluronan in wound repair. *Wound Repair Regen*. 1999; 7: 79–89.
4. Harty M, Neff AW, King MW, Mescher AL. Regeneration or scarring: an immunologic perspective. *Dev Dyn*. 2003; 226: 268–79.
5. W. Y. J. Chen and G. Abatangelo. Functions of hyaluronan in wound repair. *Wound Repair and Regeneration*. 1999; 7(2):79–89.
6. K. Harding. Clinical Challenges and Promises of HYAFF Technology in Wound Healing Redefining Hyaluronan. *Elsevier BV*. 2000.
7. Anika Therapeutics, S.r.L. Hyalomatrix 510(k) K073251. FDA Department of Health and Human Services. May 19,2011.
8. Gravante G, Sorge R, Merone A, et al. Hyalomatrix PA in burn care practice: results from a national retrospective survey, 2005 to 2006. *Ann Plast Surg*. 2010 Jan;64(1):69-79.
9. Caravaggi C. Safety and efficacy of a dermal substitute in the coverage of cancellous bone after surgical debridement for severe diabetic foot ulceration. *EWMA Journal*. 2009;9(1).
10. Onesti MG, Fino P, Fioramonti P, Amorosi V, Scuderi N. Reconstruction after skin cancer excision through a dermal induction template: our experience. *Int Wound J*. 2014 Mar 31. doi10.1111/iwj.12255.
11. Vindigni V, Bassetto F, Abatangelo S, et al. Temporary coverage of a forehead defect following tumor resection with a hyaluronic acid biological dressing: a case report. *Ostomy Wound Manage*. 2011 Apr;57(4):56-60.

*Hyalomatrix, Medline Industries Inc.

**Versatel One, Medline Industries Inc.

This study was sponsored by:

Educare™ wound & skin care education

The clinical education division of MEDLINE

MKT1550868/LIT041WC/2M/K&M7

Evaluation of the use of a hyaluronic acid based wound dressing with a silicone fluid transfer dressing

INTRODUCTION

Over the past two decades, the connection between early granulation tissue formation followed by the synthesis or presence of an extracellular matrix and the healing of full thickness dermal wound has been a major discovery.[1] This understanding has resulted in the development of synthetic and natural connective tissue matrices for managing these wounds.

Wound healing starts with platelet activation, which initiates the cascade of inflammation and progresses towards fibroblast activation and the production of hyaluronic acid (HA), glycoproteins, proteoglycans, and collagen fibers for the extracellular matrix (ECM). The major component of the ECM that is present in almost all tissue is HA,[2,3] a glycosaminoglycan characterized by a highly polymerized chain of glucuronic acid and N-acetylglucosamine units. The physicochemical and biological properties of HA allow it to interact with other ECM components and participate in a wide range of cell surface receptor interactions.[4]

The natural wound management properties derived from HA led to the design of a HA-based wound dressing. In tissue engineering and wound dressing development, benzyl esters of hyaluronic acid (HYAFF) have been extensively studied because HA derivatives show different degradation profiles.[5,6] The HA-based wound dressing is a bi-layered, sterile, flexible, and conformable wound dressing that acts as an advanced wound care device. It is comprised of a nonwoven pad entirely composed of HYAFF 11, a benzyl ester of HA, and a semipermeable silicone membrane, which controls water vapor loss, provides a flexible covering for the wound surface, and adds increased tear strength to the device. The HYAFF 11 wound contact layer biodegradable matrix acts as a scaffold for cellular invasion and capillary growth. It is indicated for the management of wounds including partial and full-thickness wounds, second degree burns, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undetermined wounds, surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, skin tears), and draining wounds.[7]

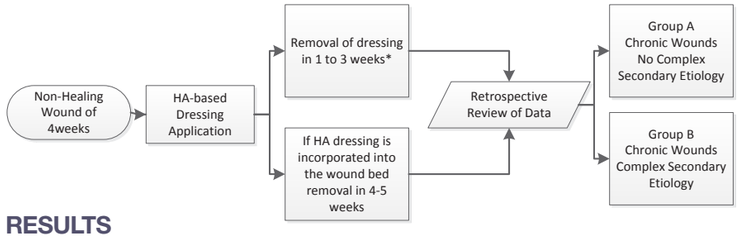
Based on a review of preliminary data, the HA-based wound dressing has been used on a variety of wounds, from burns to surgical excision wounds to diabetic foot ulcers.[8-10] It has been used to help manage deep partial thickness burns, some of which also underwent grafting.[8] In patients with diabetic foot ulcers submitted to aggressive debridement with residual bone exposition, complete coverage of the exposed cancellous bone was achieved in most of the patients following the use of the HA-based wound dressing.[9] After skin cancer excision, the HA-based wound dressing was applied on patients with complex clinical conditions, and complete healing was achieved in 8 weeks.[10] From an aesthetic perspective, the skin was smoother, and there were only minor occurrences of hypertrophic and retracted scars, but the healed skin demonstrated flexibility.[10] Furthermore, following the surgical removal of an ulcerated squamous cell carcinoma, the HA-based wound dressing integrated into the wound, and there was no evidence of hypertrophy or excessive scarring.[11] Thus it is abundantly clear that HA has been known for many decades in wound healing research to help manage wounds by providing an environment conducive to natural wound healing.

To further examine the use of a novel HA-based wound dressing*, the product was evaluated on nine patients with recalcitrant wounds. The goal of the study was to leave the dressing intact for several weeks to allow for optimal epithelialization of the wound bed. This study also provided an opportunity to investigate a non-adherent silicone transfer dressing**, to insure that the HA-based wound dressing and corresponding new growth of epithelial tissue remained intact during the dressing change process associated with the periodic removal of a secondary dressing that is typically used to collect excess wound drainage.

METHODS

A single application* of a HA-based wound dressing was evaluated in a case series of patients who presented with wounds that had not improved in the 30 days prior to dressing application. Nine patients whose wounds met the indications of use criteria were selected for the study. The study period varied from one to five weeks. Prior to product application, the wounds were optimally debrided. The HA-based wound dressing was then placed on the wound (according to the manufacturer's instructions for use) and covered with a one sided silicone transfer dressing for additional protection to ensure the secondary dressing, a silver alginate, did not disturb the wound upon removal, and steri strips were used to mechanically secure the dressing. When necessary, a no-sting cyanoacrylate liquid skin protectant was applied to the edges of the wound to aid with mechanical securement. Four or six weeks prior to application and upon initial application, the wound size was measured. Every week, the secondary absorbent dressing was changed. The primary observations for this study completed at the removal of the HA based dressing included measurements of the wound surface area and the remanding amount of epithelization. Secondary observations include time to incorporation of the dressing to the wound and examination for adverse events.

Though all patients are considered in the same HA based dressing application cohort, patients with non-healing wounds along with complex etiologies were for discussion placed in group A. Those patients with chronic wounds (but with no or less significant etiologies) were placed in group B.



RESULTS

The first group (group A) with chronic non-healing wounds (of 2.2 months average duration) in this cohort had no or less complex etiologies. This population consists of a wide variety of primary etiologies including surgical, pressure, diabetic, venous, and failed flap related wounds. Regarding demographics this population consists of all but one male with an average of 67 years of age.

This group achieved an average 89% surface area closure rate (2 completely healed) and an additional 57% of epithelization visualized over the remainder of the wound bed. This noted after a 3.8 week application time of the HA-based wound dressing. The initial goals in the study of this group was to remove the dressing at 3 weeks, but patients 3 (4 weeks on), 7 (5 weeks on), and 9 (4 weeks on) each had the dressing incorporated into the wound bed. The author allowed the dressings to remain until the HA dressing had finally separated from the closed or fully epithelized wound bed.

Table: HA wound dressings with chronic wound condition patients (Group A)

	Secondary Etiology	Chronicity	Time on	SA reduction	Additional Epithelialization
Patient 1	Noncontributory	3 months	3 weeks	69%	70%
Patient 3	Chronic DVT	1 month	4 weeks*	98%	100%
Patient 6	DM2	4 months	3 weeks	78%	0%
Patient 7	Surgical	1 month	5 weeks	100%	N/A Closed
Patient 9	Charcot arthropathy	2 Months	4 weeks	100%	N/A Closed

*Patient 3 required a second application of the HA-based wound dressing after one week because on removal of the outer tape, the silicone transfer dressing and the HA-based wound dressing were pulled up.

SA= Surface Area

Group A: Demographics & Wound Related Information

	Age/Gender	Primary DX	Location	Prior Tx
Patient 1	82yo male	VLU	R Ankle	Collagen
Patient 3	57yo male	Failed Flap	L Foot	Collagen
Patient 6	65yo male	DM2	L Leg	Honey
Patient 7	59yo female	Surgical	L Leg	Honey, Collagen
Patient 9	80yo male	PU	R Foot	Collagen

VLU: Venous Leg Ulcer, R: Right, L: Left, DVT: Deep Vein Thrombosis, PAD: Peripheral Artery Disease, BKA: Below the Knee Amputation, PU: Pressure Ulcer

The second group (group B) with an average age of 67 (2 male & 2 female) has primary wounds consisting of a two venous leg ulcers, one surgical wound, and one pressure ulcer. These in themselves are not overly complex primary wound etiologies. However, combined with complex secondary etiologies including scleroderma (1 patient), rheumatoid arthritis (1 patient), and arterial disease (2 patients) creates a different picture. This patient population suffered with non-healing wounds for over a 5 month timeframe. The HA-based wound dressing was placed and secured on the wounds of this group for an average of 2 weeks. Patients who had the dressing applied for only one week were beyond that point unable to return to the clinic (moving back to summer homes). While the wound surface area in these wounds closed on average at 44%, there was an additional 74% of epithelialization on the remaining open wound.

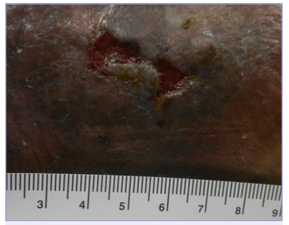
Table: HA wound dressings with complex wound etiology patients (Group B)

	Secondary Etiology	Chronicity	Time on	SA reduction	Additional Epithelialization
Patient 2	**Scleroderma**	4 months	2 weeks	0%	95%
Patient 4	**Arterial Disease**	8 months	4 weeks	90%	100%
Patient 5	**Rheumatoid Arthritis**	2 months	1 week	46%	100%
Patient 8	**Arterial Disease**	6 months	1 week	39%	0%

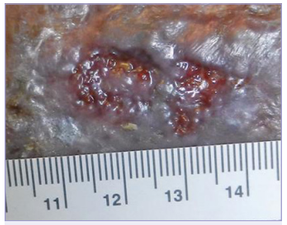
Table: Group B Demographics & Wound Related Information

	Age/Gender	Primary DX	Location	Prior Tx
Patient 2	63yo male	VLU	L Ankle	Silver Alginate
Patient 4	69yo female	Surgical	L Ankle	Silver Alginate
Patient 5	78yo female	VLU	R Leg	Foam
Patient 8	57yo male	PU	L BKA	Silver

Patient 1

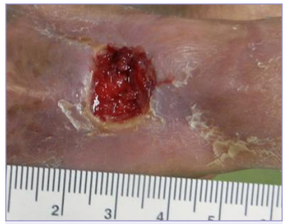


4/15/2014 First application

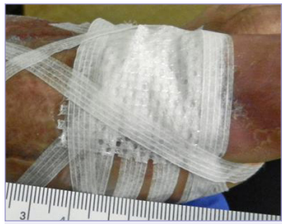


5/6/2014 Dressing Removal

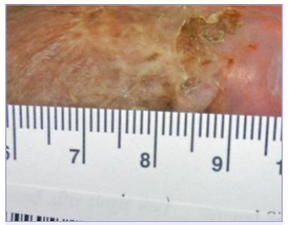
Patient 3



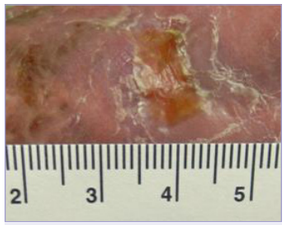
4/22/2014 First Application



4/22/2014 Dressing Application

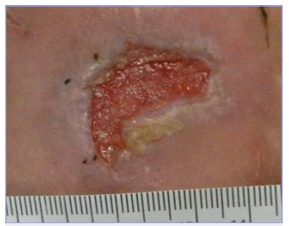


5/20/2014 Dressing Removal

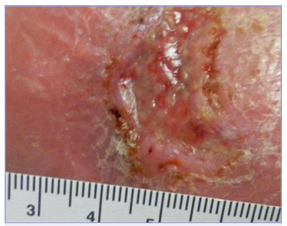


5/27/2014 Healed

Patient 4



4/22/2014 Dressing Application



5/27/2014 Dressing Removal

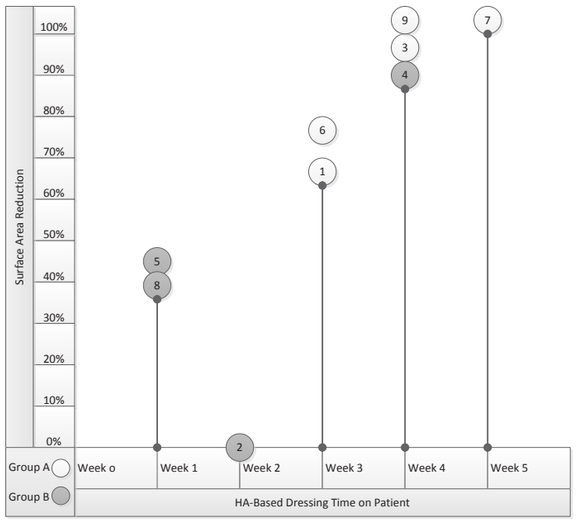


Figure 1: Wound Surface Area over Time (By Group)

As shown in Figure 1, in group B, the surface area reduction was limited related to the complex secondary etiology and the short period of time the HA-based dressing was on each wound. The length of time on the patient and simple (primary and secondary) wound etiology contributed to a significant reduction in surface area for the patients of group A.

DISCUSSION

It was the intent of the author to study the use of this product not only with chronic wounds, but also with multiple complex wound etiologies. The chronic non-healing wound group (A), of on average 2.2 month duration, had an 89% surface area closure rate with the application of the HA-based wound dressing. Chronic non-healing wounds in patients with complex secondary wound etiologies (group B) of an average a 5 month duration, had as a group a 44% surface area closure rate with the application of the HA-based wound dressing. Two significant variables in the outcomes of this patient group would be the complex patient etiologies along with a shorter average application time of the dressing at 2 weeks versus just short of 4 weeks in the other. The author believes that regardless of their complex secondary etiologies the patients in group B may have had better outcomes in terms of surface area reduction. These results, moreover, speak to the need for longer application times or multiple applications of the HA-based wound dressing for complex etiology patients.

For all patients, the silicone transfer dressing was used for additional protection to ensure the secondary dressing did not disturb the wound upon removal, and since the silicone transfer dressing is non-adherent, the epithelized tissue was not damaged on removal. In all of the case studies, no maceration was seen, and the HA-based wound dressing remained intact and in place while the HA incorporated into the wound bed. No adverse reaction to the HA-based wound dressing was observed.

CONCLUSION

Together (Group A and B) all the patients, except patient 2, experienced a reduction in wound size. Overall, there was a significant decrease in wound size ($p = 0.009$). The average reduction in wound size was 68.90%, and the wounds of patients 7 and 9 closed completely. Of the patients available for measurement one month after removal of the HA-based wound dressing , patient 3's and patient 6's wounds closed within a month post HA-based wound dressing backing removal. The majority of wounds were set on a healing trajectory after a single HA-based wound dressing application. No adverse reaction to the HA-based wound dressing was observed. For all patients, the HA-based wound dressing was securely place, and it did not damage epithelized tissue on removal.