AN IN VIVO EFFICACY EVALUATION OF VARIOUS WOUND MANAGEMENT PRODUCTS FOR THEIR RELATIVE DEBRIDEMENT ACTIVITY, USING A PORCINE WOUND ESCHAR MODEL.

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Abstract

Productive debridement is critical for the care and support of the healing of chronic wounds. However, there is a shortage of comparative data on the efficacy of various products and technologies with debridement potential, currently available on the market. In order to expand the understanding of how different products can affect wound debridement, a study was conducted using a porcine, full-thickness burn model, which has previous been reported in the literature. [Shi, L; et al 2009]

In this model, a series of twenty, 2cm, full-thickness burn wounds were created on the backs of pigs. Immediately after the burns were created, a variety of different products were applied to the eschar using a split-back study design. Using a time-course study design, debridement of the burn eschar was evaluated by clinical (visual) assessment. Depending on manufacturers' recommendations, products were re-applied either every 24 hours or every 72 hours.

The results of this study demonstrate clear differences in the debridement activity of the various products tested, highlighting the utility of this animal model as a tool for screening debridement technologies in a pre-clinical setting.

Methods

Surgery

On Day 0, each pig was premedicated by intramuscular injection of atropine (0.5 mg/kg) (1/120, Sparhawk Laboratories Inc) and anesthetized with Telazol (Tiletamine/Zolazepam; 5mg/kg, intramuscular; (Fort Dodge Animal Health, Fort Dodge, IA), followed by masked inhalation of Isoflurane USP mixed with 2-5% oxygen. Following premedication, a small portion of the caudal dorsum and the dorsal and lateral thorax of the pigs were clipped with a # 40 Oster clipper blade and washed with soap. The pigs were then transferred to the surgical suite where general anesthesia continued.

Once in the surgical suite, the pigs were prepared for surgery using a chlorohexadine scrub and isopropyl alcohol in an alternating fashion three times to mimic the skin preparation in humans and the treatment site. Twenty (20) full-thickness wounds (20 mm diameter) were created using a heated brass rod with a diameter of 2-cm, 2-cm apart; 10 per side of pig. The brass rod was heated to 100C by immersion in water at a rolling boil.The brass rod was removed from the boiling water and dried quickly but thoroughly prior to placing it on the skin surface. The heated brass rod was placed on the surface of the skin for 45 seconds to create a third degree burn. **No surgical debridement occurred after burning**

Treatments

Pig 1 - Dressing changed every 72 hours

Left Side: Antimicrobial dressing moistened: Antimicrobial dressing dressing was placed directly over the wound overlapping the outer edges of the wound by ¼" to ½".
Antimicrobial dressing was covered with 4 layered gauze and taped in place

Right Side: Moistened Control dressing

Pig 2 - Dressing change every 24 hours

Left side: Enzymatic debrider covered with dry gauze

Right side: Enzymatic debrider covered with moist Antimicrobial dressing dressing placed directly over the wound overlapping the outer edges of the wound by ¼" to ½".
Antimicrobial dressing was covered with 4 layered gauze and taped in place

Pig 3 - Dressing change every 24 hours

Left side: Honey dressing covered with dry gauze
Right side: Moistened Control dressing

Antimicrobial dressing was applied according to manufacturer's instructions, and was changed at each dressing change day.

Post Surgical Management

All wounds were covered with a blue-absorbent pad (Underpad Durasorb (Covidien)) this is the secondary dressing. **The occlusive layer of the blue pad was placed against the skin.**

- The blue pad was changed to the absorbent side against the skin if the wounds looked too wet (Optional, after day 7).
- The pigs were wrapped with a layer of elastic bandage over the blue pad to prevent movement of the dressings underneath.

Pain Management

To relieve post –wound pain (Day 0), Buprenorphine (0.005-0.02mg/ kg, IV) was administered, and a Fentanyl patch (50ug/hr) (Fentanyl transdermal system, PAR Pharmaceutical Co .Inc, Spring Valley, NY) was secured to shaved skin as post-surgical pain management, and was replaced every three days throughout the duration of the study.

Dressing Changes and treatment

- Pig 1: D0, D1, D4, D7, D10, D13
- Pigs 2 & 3: Daily, D0-D13

Assessment

Measurements of Eschar, Erythema and Edema were made via visual (clinical) assessments on the following study days. D0, D1, D4, D7, D10, D13 and D14

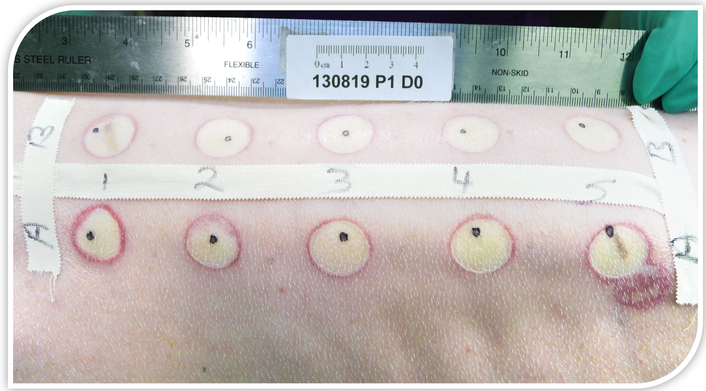
Physical Observations

Wound Measurements: For each wound, the calipers were used to measure the distance across the widest part of the wound as well as the narrowest part of the wound. The estimated wound area was calculated by using the equation for an ellipse (narrowest x widest)

Euthanasia

At the conclusion of the experiment, the experimental animal were euthanized. Euthanasia was performed by the attending veterinarian, or designate, following sedation with Telazol (4-6 mg/kg). Euthanasia was by intravenous injection of Pentobarbital Na, 110 mg/kg (Euthasol®, Diamond Animal Health, Inc., Des Moines, IA).

Figure 1: Day 0 burn eschar prior to treatment
(Note: numbers and letters are for internal data tracking, only)

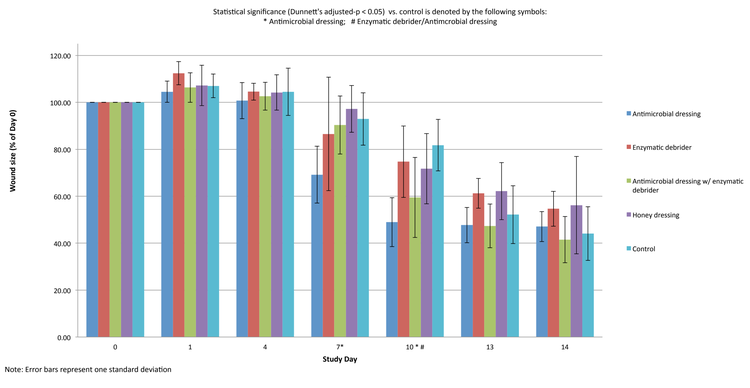


Results

Antimicrobial dressing, both alone and in combination with Enzymatic debrider, shows autolytic debridement activity in this porcine burn model. Wound healing assessments demonstrated some differences in healing rates between test and control dressings. A Student's t-test was performed to allow pairwise comparisons of all test articles against the control dressing (p-values adjusted via Dunnett's test). The results of that analysis can be found in Figure 2, below.

Analysis of the visual (clinical) assessments (Tables 1-3) suggests that the Antimicrobial dressing, both alone and in combination with Enzymatic debrider, resulted in a lower percentage of wound eschar when compared to the control. Furthermore, all of the products tested were non irritating and generated little or no swelling. Analysis was performed via a hierarchical linear model.

Figure 2. Wound size as percentage of Day 0
(100%= No healing, 0%= Complete healing)



Note: Error bars represent one standard deviation

Tables 1-3: Median values for clinical assessments of the presence of eschar, erythema and edema, respectively.

Table 1: Eschar							
Day	0	1	4	7	10	13	14
Antimicrobial dressing	5	5	5	4	4	3	2
Enzymatic debrider	5	5	5	5	4	4.5	5
Enzymatic debrider/ Antimicrobial dressing	5	5	5	5	3	2	2
Honey dressing	5	5	5	5	4	4	5
Control dressing	5	5	5	5	5	5	5

Presence of Eschar

1 = No evidence of eschar formation
2 = Eschar covering ≤ 25% of wound area
3 = Eschar covering 26 – 50% of wound area
4 = Eschar covering 51 – 75% of wound area
5 = Eschar covering 76 - ≤100% of wound area

Table 2: Erythema							
Day	0	1	4	7	10	13	14
Antimicrobial dressing	1	1	1	1	1	2	1.5
Enzymatic debrider	1	1	1	1	1	2	1
Enzymatic debrider/ Antimicrobial dressing	1	1	1	1	1	2.5	2
Honey dressing	1	1	1	1	1	2	1
Control dressing	1	1	2	1	1	1	1

Erythema

1 = No erythema (normal)
2 = Slight erythema
3 = Moderate erythema
4 = Severe erythema
5 = Very severe erythema

Table 3: Edema							
Day	0	1	4	7	10	13	14
Antimicrobial dressing	1	2	2	2	2	1	1
Enzymatic debrider	1	2	1	2	2	1	1
Enzymatic debrider/ Antimicrobial dressing	1	2	2	1.5	2	1	1.5
Honey dressing	1	2	1	1	2	2	1
Control dressing	1	2	2	2	2	1.5	1

Edema

1 = No edema (normal)
2 = Slight edema
3 = Moderate edema
4 = Severe edema
5 = Very severe edema

Figure 3: Day 14 burn eschar that has been treated with honey. Eschar is still intact.
(Note: numbers and letters are for internal data tracking, only)

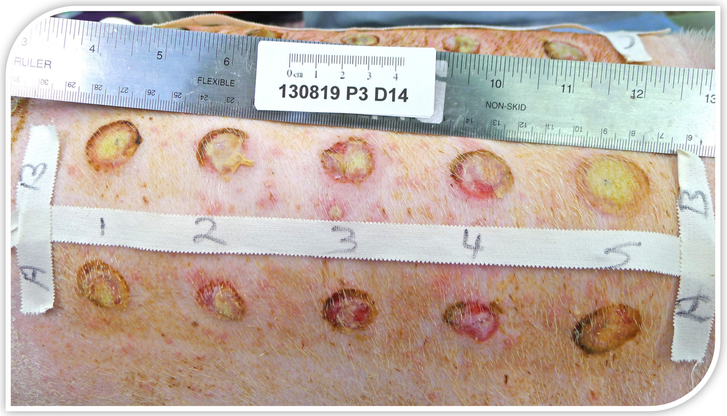
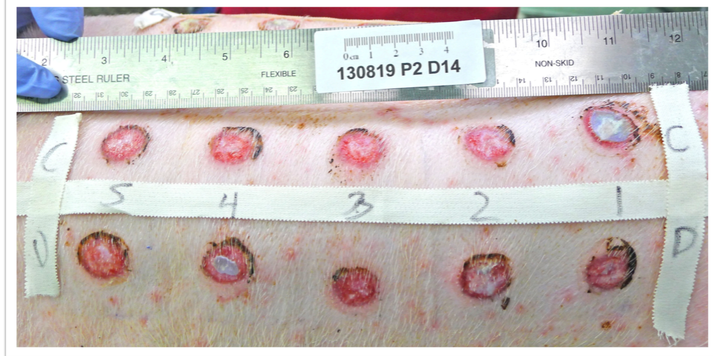


Figure 4: Day 14 burn eschar that has been treated with Antimicrobial dressing and Enzymatic debrider. Eschar is almost completely debrided.
(Note: numbers and letters are for internal data tracking, only)



Conclusions

Using amount of eschar as the primary clinical endpoint, Antimicrobial dressing and Antimicrobial dressing with Enzymatic debrider were more effective than the other products and controls evaluated in this porcine, burn-eschar model. All products and controls were equally non-irritating..

References

1. **Study on the debridement efficacy of formulated enzymatic wound debriding agents by in vitro assessment using artificial wound eschar and by an in vivo pig model. Shi L, Ermis R, Lam K, Cowart J, Attar P, Aust D. Wound Repair Regen. 2009 Nov-Dec;17(6):853-62. doi: 10.1111/j.1524-475X.2009.00545.**

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Antimicrobial dressing = Hydrofera Blue™, Hydrofera, LLC.
Enzymatic debrider = Santyl Collagenase® Ointment, Smith & Nephew
Honey dressing = MediHoney, Wound and Burn Dressing, Derma Sciences
Control = Telfa™ ("Ouchless" Non adherent Pad", Kendall)