Comparative Evaluation of Commonly Used Antimicrobial Wound Dressings and Nitric Oxide Treatment of Infected and Non-Infected Full-Thickness Wounds on Swine (Sus scrofa)

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OBJECTIVE

Develop an evidenced-based uninfected and CA-MRSA exposed full-thickness wound model on swine (Sus scrofa). Inform the medical community of best practices for wound healing, comparing the non-antibiotic antimicrobial dressings Aquacel Ag, Hydrofera Blue, Medihoney Calcium Alginate, wet-to-dry Dakin’s hypochlorite solution-soaked gauze, and saline-soaked gauze (control). With best practices identified in the established models, evaluate topical nitric oxide delivering advanced development candidate technologies.

ABSTRACT

Skin and soft tissue infections (SSTI) represent nearly $25 billion in U.S. annual medical costs. Drug-resistant bacteria pose a dire threat to public health, and the alarming dearth of new antibiotics compels the characterization of novel, pre-healing, broad-spectrum antimicrobials. To better inform wound care providers, we developed evidenced-based full-thickness uninfected and commonly exposed MSSA- and CA-MRSA-exposed full-thickness wound models on swine to test wound healing and post-exposure prophylactic antimicrobial efficacy of Commercial-off-the-Shelf (COTS) antimicrobial dressings. With best practices identified, we comparatively challenged the performance of topical PhoGel48 containing nitric oxide (NO) delivering advanced development technology developed under US Army SBIR contract W81XWH-11-C-00029. We hypothesized that compared to wet-to-dry dressings, NO delivering wound healing and antimicrobial activity versus the FDA approved treatments tested, and potentially meet a critical need for improved SSTIs. Of all test groups, only the NO-releasing drug groups were capable of providing improved antimicrobial activity versus wet-to-dry gauze controls, and were not contraindicated for wound healing. The linear wound healing measurements of PhoGel48 (0.3% NO) was statistically superior to saline control (p < 0.05).

METHODS

Post-Exposure Prophylaxis Full-Thickness Wound Healing Model

Evidenced-Based Wound Healing Evaluation of Antimicrobial Treatments

COTS Comparison

1. Aquacel Ag (21.2 cm long, 2.5 cm wide)
2. Hydrofera Blue (21.2 cm long, 2.5 cm wide)
3. Medihoney Calcium Alginate (8 x 8 cm)
4. Dakin’s hypochlorite 1.25% iodine incorporated (5 x 5 cm)
5. Tegaderm® for control

Underwound Full-Thickness Wounds

Deep Dressing Changes

1. COTS Phantom dressings: Hydrofera Blue and Medihoney Calcium Alginate, and saline-soaked dry gauze changed daily.
2. PhoGel48 Phantom: Hydrogauze changed every three days, or when changed, as needed.

Evaluation Metrics:


Study Strength

COTS Comparison Evaluation: n = 6
PhoGel48 Evaluation: Limb x 2
Exposure: n = 3

RESULTS

Figure 3. Linear Wound Healing calculated using the Gilman’s Equation for COTS Comparison (left) and PhoGel48 Evaluation (right).

Figure 4. Representative wounds on day 10 (photograph, left). Uninfected PhoGel48 animal displayed. Tattooed areas are the original wound area (minus any contraction). Red areas considered final wound areas. Treatment groups: H = Hydrofera Blue, S = Saline, D = Dakin’s, N = NO PhoGel48.

Figure 5. Wound contraction calculated by the change in tattooed wound area for COTS Comparison (left) and PhoGel48 Evaluation (right).

DISCUSSION

The rise of hospital-acquired SSTIs involving Multi Drug-Resistant Organisms (MDRO) and the alarming shortage of new antimicrobial treatments compel the identification of best wound care practices, and the discovery of novel non-antibiotic therapeutic approaches. Our data suggest that COTS product choice should include consideration for infection risk mitigation, and the efficiency of wound healing. The COTS tested here versus wet-to-dry Saline- or Dakin’s gauze are neither contraindicated for wound healing, or are not effective microbial proliferation suppression agents. Our post-hoc data analysis demonstrates that multiple wet-to-dry dressing changes per day may aid in removal of surface microbes; the practice does not accelerate wound healing. Interestingly, we observed that the small population of heavily bleeding, highly vascular animals were statistically superior for wound healers versus the remaining subject population.

We find significant promise in the exploration of broad-spectrum anti-microbial treatments based on topical nitric oxide, which also provide accelerated pro-healing benefits. The PhoGel48 product developed under Army SBIR and tested in this work should be challenged with an expanded panel of single- and poly-MDRO exposures for its non-antimicrobial efficacy and wound healing performance.

CONCLUSIONS

- Aquacel Ag and Hydrofera Blue antimicrobial dressings are contraindicated for wound healing versus control.
- Of COTS compared to Saline, only Dakin’s solution-soaked wet-to-dry gauze provided both comparable levels of wound healing and suppression of microbial proliferation.
- There is no wound-healing benefit to multiple wet-to-dry dressing changes in a single day.
- Both PhoGel48 0.3% and 1.8% nitric oxide delivering formulations appear to have enhanced post-MRSA and CA-MRSA eradication properties, a formulation providing suppression in the uninfected model.
- The PhoGel48 0.3% nitric oxide delivering compound was the only treatment to demonstrate improved linear wound healing versus Saline-soaked wet-to-dry gauze.
- Highly vascular subjects demonstrated significantly accelerated wound healing in these studies.