Antimicrobial Effects of a Novel Combination Therapy Against Methicillin-Resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* in a Porcine Wound Model

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Introduction

- Chronic wound infections contain various species of bacteria, primary among which are *Staphylococcus aureus* and *Pseudomonas aeruginosa* (PA)[1,2]
- The degree of microbial growth, especially biofilm formation, has a direct impact on wound healing[3]
- Therefore, limiting bacterial growth is an essential component of chronic wound care
- A novel technology has been designed to target components of wound healing in chronic or refractory wounds, regardless of pathology
- The combination therapy consists of formulations that address wound preparation, wound therapy (OCM™), and skin integrity

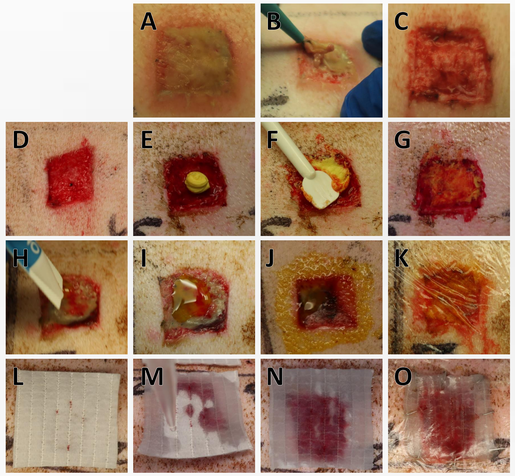
Objective

- To evaluate the antimicrobial and wound-healing effects of various wound care formulations against methicillin-resistant *Staphylococcus aureus* (MRSA) and PA using a porcine wound model

Methods

- Thirty-one deep reticular wounds (22 mm × 22 mm × 3 mm) were made across the paravertebral and thoracic areas on each of 6 specific pathogen-free pigs (Looper Farms, North Carolina)
- Pathogenic strains of MRSA (USA300) or PA (ATCC 27312) prepared as 10^6 CFU/mL inoculum suspensions were used to inoculate all wounds within 20 minutes after wounding
- Inoculated wounds were covered with polyurethane dressings (Tegaderm, 3M, USA) for 72 hours before being treated
- Treatment consisted of OCM alone, OCM plus skin protectant, or Aquacel Ag Advantage (positive control) or wounds left untreated (negative control)
  - Wounds treated with OCM alone were debrided before treatment and covered with polyurethane dressings (**Figure 1, A-G**)
  - Wounds treated with OCM plus skin protectant received a wound preparation formulation for 3 minutes before debridement, were debrided, were treated with OCM and skin protectant, and were covered with polyurethane dressing (**Figure 1, H-K**)
  - Wounds treated with Aquacel Ag Advantage were initially debrided, treated with Aquacel, and covered with polyurethane dressing (**Figure 1, L-O**)
  - Untreated wounds were debrided then covered with polyurethane dressing
- All treatments (except wound preparation) were reapplied on Days 4 and 8
- Baseline wounds were biopsied before and after debridement, and baseline counts were obtained on Day 0; treated wounds were assessed on Days 4, 8, and 12 after treatment

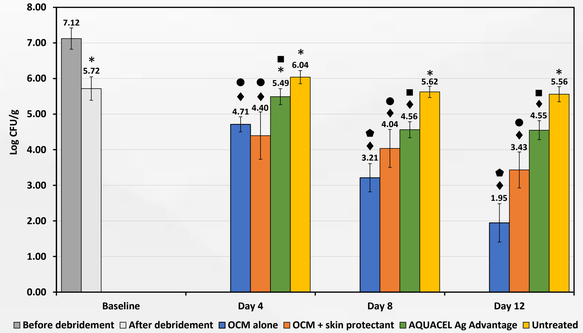
Figure 1. Wound preparation and application of OCM, OCM plus skin protectant, and Aquacel Ag Advantage



Results

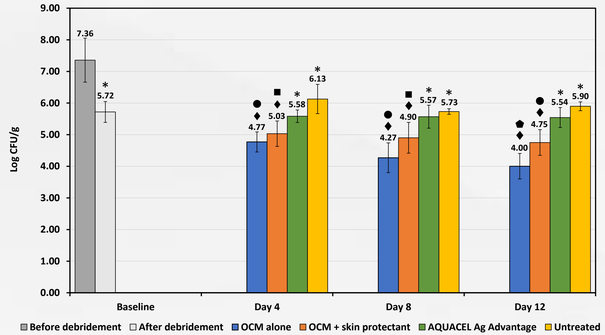
- On Days 8 and 12, MRSA USA300 counts were significantly lower in OCM alone-treated wounds versus all other treatments (**Figure 2**)
- On Days 4, 8, and 12, MRSA USA300 counts were significantly lower in wounds treated with OCM plus skin protectant versus those treated with the positive and negative controls (P≤0.05, all comparisons; **Figure 2**)
- On Days 4, 8, and 12, PA27312 counts were significantly lower in wounds treated with OCM alone or OCM plus skin protectant versus baseline before and after debridement (P≤0.05, all comparisons; **Figure 3**)
- Day 12 PA27312 counts were significantly lower with OCM alone versus all other treatments and with OCM plus skin protectant versus Aquacel and untreated control (P≤0.05, all comparisons; **Figure 3**)
- Among all treatments at all time points, the lowest MRSA USA300 and PA27312 counts occurred on Day 12 in wounds treated with OCM alone (**Figures 2** and **3**)
- On Day 8, increased granulation in MRSA USA300-infected wounds was observed with OCM alone compared with OCM plus skin protectant (**Figure 4**)
- Compared with Aquacel-treated wounds, MRSA USA300-infected wounds treated with OCM plus skin protectant showed increased re-epithelialization on Days 4 and 8 (**Figure 5**)
- In PA27312-infected wounds, increased re-epithelialization was observed with Aquacel compared with OCM alone at Day 4, and increased granulation was observed with Aquacel compared with OCM plus skin protectant at Day 8

Figure 2. MRSA USA300 bacterial counts after treatment application at each assessment day.



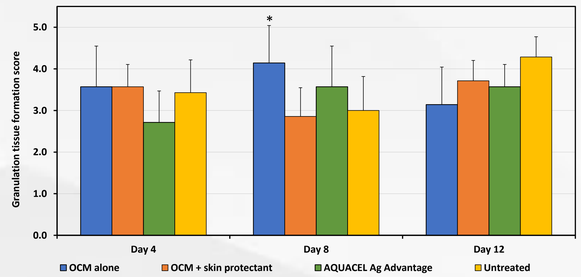
*P≤0.05 vs. Baseline before debridement
●P≤0.05 vs. Aquacel Ag Advantage and Untreated control
◆P≤0.05 vs. Baseline before/after debridement
●P≤0.05 vs. All treatments
■P≤0.05 vs. Untreated control

Figure 3. PA27312 bacterial counts after treatment application at each assessment day.



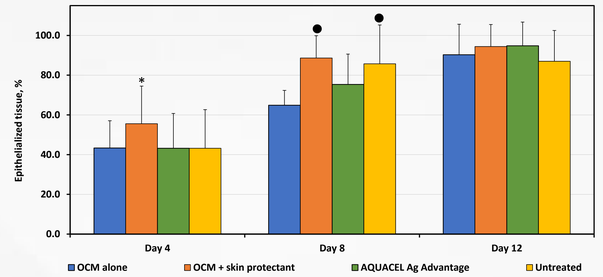
*P≤0.05 vs. Baseline before debridement
●P≤0.05 vs. Aquacel Ag Advantage and Untreated control
◆P≤0.05 vs. Baseline before/after debridement
●P≤0.05 vs. All treatments
■P≤0.05 vs. Untreated control

Figure 4. Granulation tissue formation in MRSA USA300-infected wounds at each assessment day.



*P≤0.05 vs. OCM plus skin protectant

Figure 5. Re-epithelialization of MRSA USA300-infected wounds at each assessment day.



*P≤0.05 vs. OCM alone
●P≤0.05 vs. AQUACEL Ag Advantage

Conclusions

- OCM alone was significantly better at halting proliferation in both MRSA USA300- and PA27312-infected wounds compared with baseline before and after debridement and compared with all other treatment groups
- OCM and OCM plus skin protectant significantly reduced MRSA USA300 and PA27312 counts in this *in vivo* model, recording the lowest bacterial counts of any treatment in the study
- Compared to the other treatments, OCM alone and OCM plus skin protectant showed significantly faster formation of new tissue in MRSA USA300-infected wounds
- These findings may have important clinical implications for the management of many wound etiologies, such as burns, diabetic foot ulcers, and pressure ulcers

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DISCLOSURES

SCD, JG, MS: Research support, Omeza, LLC.
SJB, DB: Employees, Omeza.

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