Treating MRSA Infected Wounds in a Real-world Setting: Healing Outcomes of Chronic, MRSA Infected, Lower Extremity Wounds Utilizing a Treatment Protocol that Combines a Wound Dressing Containing Oakin with a Modified De-escalation Theory

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ABSTRACT

PURPOSE: The frequency of wound infections caused by the *Methicillin-Resistant Staphylococcus Aureus* (MRSA) organism continues to rise, posing a major health issue in terms of treatment strategies. A treatment protocol integrating elements of the de-escalation theory together with an Oakin antimicrobial wound dressing for lower extremity MRSA infected wounds of different etiologies is evaluated in non-controlled settings.

METHODS: A total of 40 chronic MRSA infected lower extremity wounds of different etiologies were treated in either a private practice or in a wound care center and followed for 90 days. The Oakin antimicrobial dressings were applied to all wounds daily and select participants were administered broad-spectrum oral antibiotic(s). Wound healing outcomes were assessed at 30, 60, and 90 day intervals.

RESULTS: All wounds were classified by etiology: 58% (n=23) Diabetic neuropathic ulcers (DNU), 25% (n=10) Venous insufficiency ulcers (VU), and 17% (n=7) Pressure ulcers (PU). Overall, **35% (n=14) healed within 30 days (22.14 ± 4.47), 60% (n=24) healed in 60 days (31.76 ± 13.02), and 78% (n=31) healed in 90 days (40.81 ± 22.23).**

CONCLUSION: This clinical case series demonstrates that a treatment protocol combining the de-escalation theory and an Oakin antimicrobial dressing can achieve 78% wound closure within 90 days when treating chronic MRSA infected lower extremity wounds of different etiologies in the real world. This treatment protocol is intended to provide a roadmap for clinicians to follow and adapt to their setting where a high prevalence of MRSA infected wounds exist.

INTRODUCTION

Perhaps more than any other medical specialty, wound care providers are in a unique position to more readily lessen the unnecessary use of systemic antibiotic agents to treat skin or soft tissue infections. In many situations, the use of silver or other antimicrobial formulations or specialty antimicrobial wound dressings preclude a "knee-jerk" reaction of randomly prescribing systemic antibiotic therapy until determining that a systemic or intravenous agent is indicated.[6,7] While the choice of antibiotic(s) is important, so should the choice of a topical antimicrobial dressing to cover the wound.
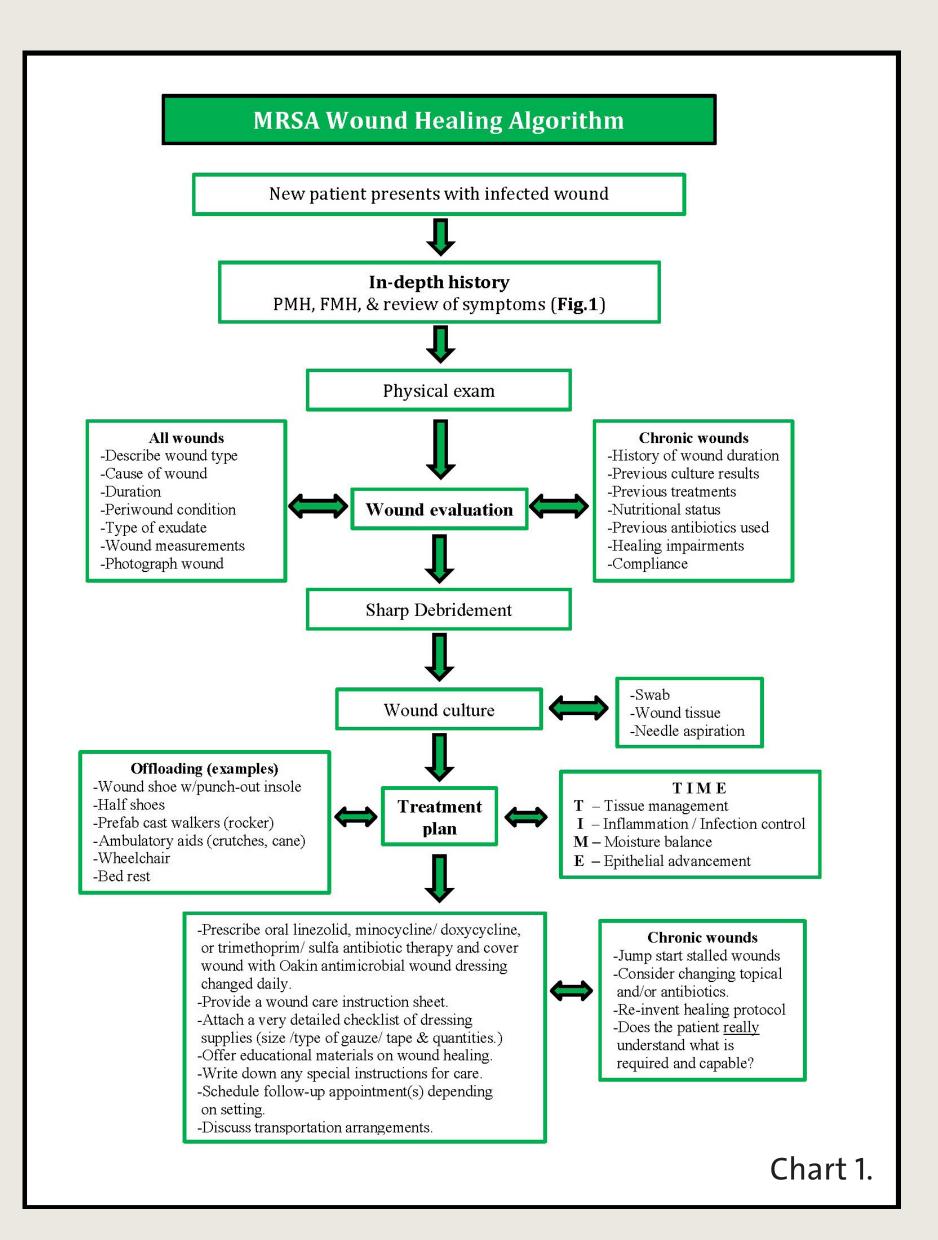
Antimicrobial agents used in current wound dressings include ionized silver, iodine, polyhexamethylene biguanide, and natural tannins.[8] Oakin, a natural tannin harvested from oak extract (AmeriGel Wound Dressing, Amerx Health Care Corp., Clearwater, FL), exerts bactericidal and fungicidal activity against 51 pathogens, including MRSA and VRE. One in-vitro time-kill study revealed the Oakin wound dressing's ability to eliminate 99.2% of MRSA in 6 hours and sustained the kill rate for the remainder of the 24 hour test.[9] Their findings suggested that there were no substantial differences in antimicrobial efficacy between Oakin and ionic silver. Moore and Perkins compared the antimicrobial efficacy and cost of Oakin to three wound dressings containing silver.[9] Their findings suggested that there were no substantial differences in antimicrobial efficacy between Oakin and ionic silver.

A MRSA Wound Healing Protocol (Protocol) was created for use in multiple settings including a wound care center or private practice. (Chart 1)[9] This Protocol not only provides a treatment plan for the healthcare provider but a step by step process to follow when evaluating and managing a new patient. The Protocol incorporates concepts of the de-escalation theory, provides the choices of empiric therapy, and utilizes the Oakin antimicrobial dressings as the primary wound cover. The effectiveness of this Protocol would be based on the overall wound healing outcomes of participants enrolled.

METHODS

A total of 40 lower extremity, MRSA infected, chronic wounds were enrolled and classified as Diabetic neuropathic ulcers (DNU), Venous insufficiency ulcers (VU), and Pressure ulcers (PU). Each wound was assessed, measured, documented, photographed, offloaded as necessary, and debrided every 7-10 days at the wound care center and every 10-14 days at the office setting. Participants and/or their caregivers were given standardized wound care instructions for daily dressing changes that explained proper cleansing of the wound, application of the Oakin antimicrobial dressing, and covering with a secondary plain gauze dressing. The Oakin antimicrobial dressings used for this article were a one ounce (30gm) tube or individually wrapped, sterile 2" x 2" saturated gauze dressings provided free of charge to each participant and used until closure.

Participants were scheduled for follow-up visits every 7-10 days at the wound care center and every 10-14 days at the office setting. For purposes of this article, no wounds were followed beyond 90 days; however the participants continued some course of treatment. Data gathered was analyzed by: gender, proportion healed at 30, 60 and 90 days, wound etiology, wound size, healing time by setting, and days to heal overall. The wound healing outcomes would demonstrate the potential effectiveness of the Protocol (Chart 1).

Chart 1.

RESULTS

The participants had treatment performed exclusively at a private practice or wound care center setting. Of the 40 participants, 43% (n=17) were seen in the private practice/office (OFC) setting and 57% (n=23) were seen in the wound care center (WCC) setting. Each participant had one chronic non-healing wound greater than 90 days duration and had a positive culture for MRSA infection. Overall, 35% (n=14) healed within 30 days (22.14 ± 4.47), 60% (n=24) healed in 60 days (31.76 ± 13.02), and 78% (n=31) healed in 90 days (40.81 ± 22.23). (Table 1) After 90 days, the remaining 23% (n=9) participants were re-evaluated, however, for study purposes their data was not followed or captured.
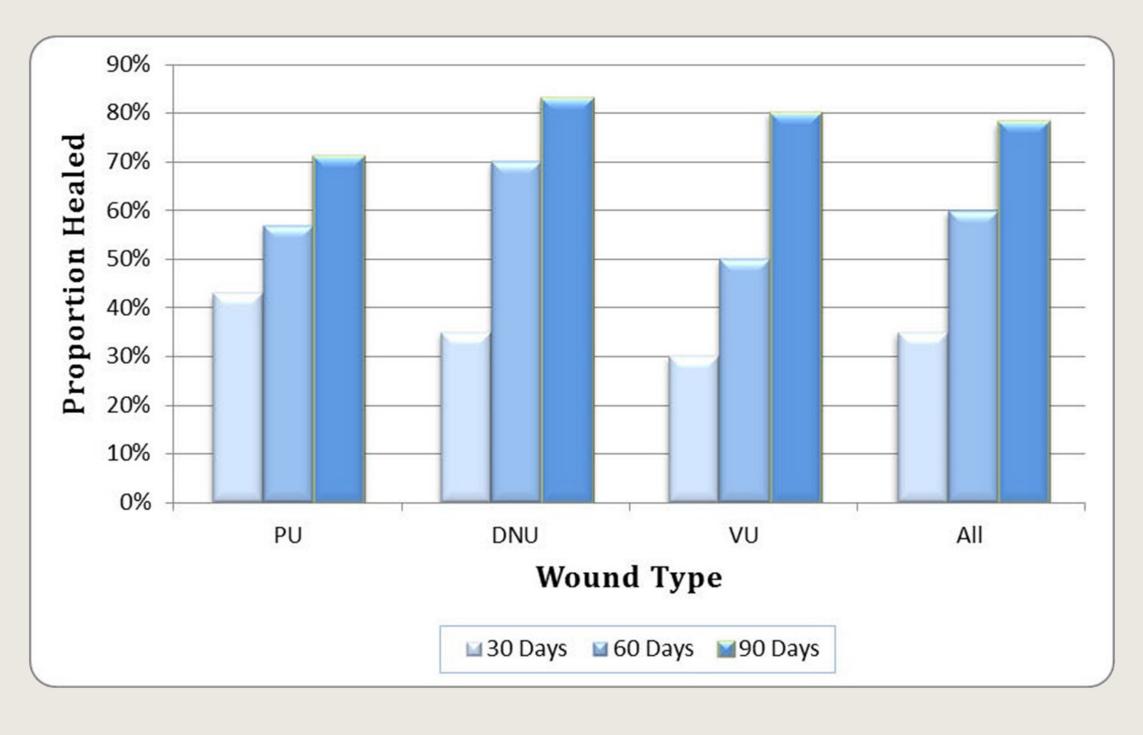

Table 1 – Proportion healed by wound type
For All wound types, 35% (n=14) healed within 30 days (22.14 ± 4.47), 60% (n=24) healed in 60 days (31.76 ± 13.02), and 78% (n=31) healed in 90 days (40.81 ± 22.23).

All wounds were classified by etiology: 58% (n=23) Diabetic neuropathic ulcers (DNU), 25% (n=10) Venous insufficiency ulcers (VU), and 17% (n=7) Pressure ulcers (PU). (Table 2) Further analysis revealed 20% (n=10) of wounds were healed at 21 days (19.40 ± 2.67), 42% (n=21) healed at 35 days (25.10 ± 6.73).

Types of Wounds	Enrolled by Setting n (%)	Age (years)	Healed at 30 days	Healed at 60 days	Healed at 90 days
DNU	OFC = 10 (43%)	68.13 ± 12.81	2 (20%)	6 (60%)	8 (80%)
	WCC = 13 (57%)	57.06 ± 11.62	6 (44%)	9 (75%)	10 (81%)
	Total = 23 (58%)	**60.75 ± 12.90**	**8 (35%)**	**16 (70%)**	**19 (83%)**
VU	OFC = 3 (30%)	71.67 ± 17.21	1 (33%)	1 (33%)	2 (67%)
	WCC = 7 (70%)	63.43 ± 9.68	2 (29%)	4 (57%)	6 (86%)
	Total = 10 (25%)	**65.90 ± 12.00**	**3 (30%)**	**5 (50%)**	**8 (80%)**
PU	OFC = 4 (57%)	69.33 ± 21.73	1 (25%)	1 (25%)	2 (50%)
	WCC = 3 (43%)	54.25 ± 18.73	2 (67%)	3 (100%)	3 (100%)
	Total = 7 (17%)	**60.71 ± 19.95**	**3 (43%)**	**4 (57%)**	**5 (71%)**
Total	OFC = 17 (43%)	69.14 ± 14.45	4 (24%)	8 (47%)	12 (71%)
	WCC = 23 (57%)	58.30 ± 12.27	10 (43%)	16 (70%)	19 (83%)
	40	**62.00 ± 13.89**	**14 (35%)**	**24 (60%)**	**31 (78%)**

Table 2 – Wound Type and Healing Time by Setting
Data shown as n (%) and mean ± standard deviation.

Of the 40 enrolled, 45% (n=18) were male and 55% (n=22) were female, ranging in age 28 to 91 years (62.66 ± 14.58). **(Table 3)**

Gender	N (%)	Age (years)	Healed at 30 days	Healed at 60 days	Healed at 90 days
Male	18 (45%)	63.00 ± 14.51	65.00 ± 15.56	63.54 ± 13.84	64.00 ± 15.10
Female	22 (55%)	61.22 ± 13.65	59.57 ± 13.13	61.25 ± 13.46	62.20 ± 13.44

Table 3 – Gender breakdown
Data shown as n (%) and mean ± standard deviation.

Case Studies – Case One

Right Lower Leg Ulcer With MRSA Infection.

HISTORY: 91 year-old Caucasian male referred from PCP with a chronic non-healing wound. PCP drained initial abscess and treated resulting wound with periodic debridements and topical Mupirocin for 18 months. (Case 1a)

TREATMENT: Debridement of wound and covered with Oakin Saturated Gauze dressing. Instructed patient to change dressing daily. Wound culture positive for MRSA.

RESULTS: Patient's wound rapidly progressed to closure. Wound culture was negative for MRSA in one week. The wound healed in 2 weeks (14 days.) (Case 1b)

Case 1a: Pre-debridement

Case 1b: Healed in 2 weeks

Case Studies – Case Two

Left Lateral Ankle Ulcer With MRSA Infection.

HISTORY: 66 year-old Caucasian female presented with non-healing ulcer over left lateral malleolus. No palpable DP or PT pulses and +2 edema. Previous ulcer of 5th right toe with revascularization. Radiographs negative for Osteomyelitis but wound culture positive for MRSA. (Case 2a)

TREATMENT: Oral Linezolid 600 mg. Wound debridements every 2 weeks and daily dressing changes with Oakin Wound Dressing. Revascularization performed 2 days after initial visit. (Case 2b)

RESULTS: Wound steadily progressed to closure. Completed full course of empirical therapy. The wound healed in 11 weeks (71 days). (Case 2c)

Case 2a: Pre- debridement

Case 2a: Pre- debridement

Case 2a: Pre- debridement

DISCUSSION

The design of a treatment protocol is dependent on multiple factors including: patient co-morbidities, the treatment setting, insurance restrictions on what treatment modalities and medications are covered, modalities that are available at treatment setting, and most important the compliance of the patient to follow a clinician's orders. Any treatment protocol should be revised periodically due to new developments in modalities, new antibiotics, complications, and many other reasons. The goal should always remain the same; to provide quality care and obtain optimal healing outcomes while practicing antibiotic stewardship. The treatment protocol created for this article has shown to be a viable option for the wound care provider to consider implementing.

De-escalation theory
The following guidance provided de-escalation concepts which were incorporated into the treatment protocol for this article: [1]
- Cultures of presumed infected site(s) should always be obtained (preferably prior to any antibiotics).
- Initial empiric therapy should be chosen based on most likely pathogens, cost-effective therapy, and impact on development of resistance.
- Patients' flora may be altered by previous antibiotic courses and recent therapy should be taken into account when choosing initial empiric therapy.
- Greater severity of illness or severely immunocompromised state may warrant broader initial empiric coverage.
- Once culture results are obtained, antibiotic therapy should be modified to target identified pathogen(s) and to narrow the Spectrum of activity if possible.

Oak technology
The Oakin antimicrobial wound dressings were chosen for this article because they do not contain any drugs which could potentially lead to a resistance. Considered hydrogels, these dressings are limited to usage on wounds that are dry and require moisture or have little to nominal drainage. A wound with copious exudate would require a different primary and secondary dressing. For this reason, the inclusion criteria required the wound to be hydrogel appropriate.

In-depth history
The risk of community associated/acquired MRSA infection is reality today. Upon initial presentation, all wounds require an in-depth history. (Figure 1) physical examination, and the assessment regardless of infection. Documentation of the wound in the medical record is essential to substantiate the treatment protocol and should include the following:
1. Location, etiology, duration, and type of wound.
2. Wound measurements by length, width, and depth.
3. Photograph the wound pre- and post-debridement.
4. Condition of the periwound skin.
5. Amount and type of wound exudate.

There were no significant relationship of age or gender to healing time noted. However, the days to heal was strongly correlated with the wound size (LxWxD cm2) r = .28, p = .002. (Table 4)

Figure 1.
OBTAIN AN IN-DEPTH HISTORY
- ✓ Current or recent hospitalization
- ✓ Living in a long term facility
- ✓ Invasive devices
- ✓ Chronic illness
- ✓ Recent antibiotic therapy within the past year – (Treatment with a Quinolone or Cephalosporin Can increase the risk of MRSA)
- ✓ The patient is of young or older age
- ✓ Participating in contact sports
- ✓ Sharing towels or athletic equipment
- ✓ Weak or compromised immune system
- ✓ Living in a crowded or unsanitary condition
- ✓ Association with health care workers
- ✓ History of MRSA infection/colonization – (29% in 18 months)[7]
- ✓ Geographic location

Table 4 – Wound Dimensions to Days to Heal
Healing time was unrelated to the type of wound, p = .61. Of the 31 participants healed in 90 days, the 71% (n=12) of the OFC setting healed in an average of 51.78 ± 25.76 days and the 83% (n=19) of the WCC setting healed in an average of 36.32 ± 19.50 days.
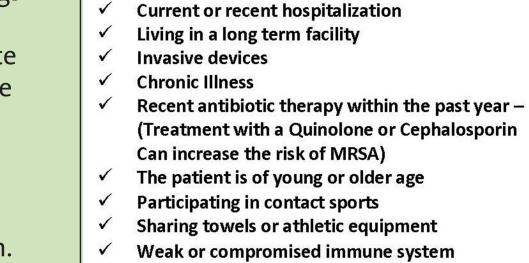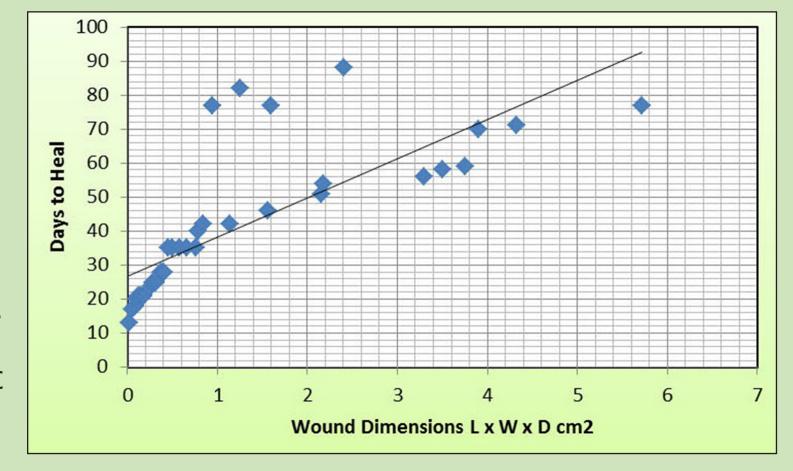
CONCLUSION

This is the first clinical case series involving the use of Oakin antimicrobial wound dressings in the treatment of chronic, MRSA infected, lower extremity wounds in a real time setting. This article was not intended to highlight the effectiveness of one product or treatment modality, rather to provide a roadmap for clinicians to follow and adapt to their setting where a high prevalence of MRSA infected wounds exist.

This article suggests the use of a treatment protocol for lower extremity MRSA infected wounds is an efficacious protocol that can achieve 35% healing within 30 days, 60% healing in 60 days and 78% healing in 90 days.

LIMITATIONS

While large randomized controlled studies comparing the Oakin antimicrobial dressings to other antimicrobial wound dressings in combination with empirical antibiotic(s) would better determine the efficacy of this treatment protocol, the results of this article continue to validate the therapeutic benefit of the Oakin antimicrobial dressings. Comparing the Oakin antimicrobial dressing to a control on a moderate to severe MRSA infected wound without the use of empirical antibiotics could pose almost certain medico-legal and ethical issues.

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