The prevalence of antibiotic-resistant bacteria such as methicillin-resistant Staphylococcus aureus is rapidly increasing in healthcare facilities and spreading to the community. Methicillin-resistant S. aureus colonize the skin and open wounds and can interfere with wound healing. Recent studies have shown that ultraviolet light C can kill antibiotic-resistant strains of bacteria such as methicillin-resistant S. aureus in both laboratory cultures and animal tissue. This clinical report describes the effects of ultraviolet light C on wound bioburden and closure in three people with chronic ulcers infected with methicillin-resistant S. aureus. In all three patients, ultraviolet light C treatment reduced wound bioburden and facilitated wound healing. Two patients had complete wound closure following 1 week of ultraviolet light C treatment. This case study suggests that ultraviolet light C is a promising adjunctive therapy for chronic wounds containing antibiotic-resistant bacteria such as methicillin-resistant S. aureus.

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known. The purpose of this case study was to evaluate the potential role of UVC in reducing wound bioburden and improving wound status in chronic ulcers infected with MRSA.

Method

UVC treatment protocol. Using an application technique that has been previously described by Nussbaum et al.,21 UVC was applied at a distance of 1 inch and perpendicular to the wound using premeasured disposable spacers. Before treatment, a 254-nm, cold quartz UVC generator, approved for clinical use in Canada (supplied by Medfaxx Inc., Raleigh, NC) was warmed for 5 minutes before being placed over the wound. The ulcer was cleansed with sterile saline, a thick layer of petroleum jelly was applied to the surrounding periulcer skin and any healthy granulation tissue, and the wound edges were covered with a drape.

The UVC generator was applied to the wound for 180 seconds per wound site. This length of time is recommended for the treatment of infected ulcers21 and was selected based on the MRSA killing rates reported in a previous in vitro study.24 To shield the eyes from UVC, the therapist and patient wore protective goggles. All products applied to the patient were sterilized or discarded after a single use. Equipment that had to be reused was decontaminated using appropriate protocols.

Subject recruitment. Approval for research involving human subjects was obtained from appropriate institutional review boards. The purpose, method, risks, and benefits of UVC treatment were explained to the patients and/or their substitute-decision makers and informed consent was obtained. Patients included in this case series had a chronic ulcer present for at least 3 months that was infected with MRSA. By definition, an infected wound has a positive swab culture and clinical signs of infection, including: marked redness extending beyond the wound margins; increased pain; and increased amounts of foul smelling, purulent wound exudates. Oral antibiotic or topical antimicrobial therapy may or may not be required.27

Outcome measures. To determine the magnitude of bacterial burden in wounds for this case study, clinicians used a standardized protocol for administering a semiquantitative swab.26-31 The lab results from the semiquantitative swab are reported as type and relative amount of bacteria present — eg, no growth (0), occasional growth (scant), light growth (1+), moderate growth (2+), or heavy growth (3+). Other outcome measures included taking photographs and assessing changes in wound appearance using the Pressure Sore Status Tool (PSST).22 The PSST is a pen-and-paper tool consisting of 13 domains that assess the composition of wound bed; wound size, depth, and exudate; and the condition of the periulcer skin and wound edge. Scores assigned on a scale of 1 to 5 to each of the individual domains of the PSST are totaled to derive a total score ranging between 13 and 65, with 13 representing a completely healed wound. The PSST has previously been shown to produce valid and reliable assessments of wound appearance.32

Case 1

A 77-year-old man had multiple leg ulcers due to a combination of venous and arterial insufficiency related to his previous occupation that involved prolonged standing. His long history of venous insufficiency included numerous corrective surgical procedures, including vein stripping. He presented with hypertension, bilateral leg edema, and significantly impaired bilateral lower extremity blood flow with ankle brachial indices (ABI) of 0.53 and 0.61 of the left and right leg, respectively. He ambulated with a cane and had limited mobility and impaired muscle pump function in both lower extremities. The extreme pain reported by this patient not only limited his mobility, but also caused significant sleep disturbances, leading to mild depression. Current medications included: pentoxifylline (400 mg tid), enalapril maleate (2.5 mg bid), and acetaminophen (500 mg qid).

KEY POINTS

- Chronic wounds are an important risk factor for acquiring antibiotic-resistant bacteria that may, in turn, delay healing.
- The case studies presented here build on and confirm earlier pre-clinical study observations: Ultraviolet light C can kill methicillin-resistant Staphylococcus aureus, as well as other non-antibiotic resistant bacteria.
- Given existing treatment limitations, current trends in the emergence of antibiotic-resistant bacteria, and the encouraging results reported here, research to ascertain the effectiveness of treatments that may help break the cycle of antibiotic resistance is long overdue.
At his initial wound evaluation in July 1998, the patient presented with a total of six large superficial ulcers located in the medial and lateral lower leg region bilaterally. These ulcers ranged in size from approximately 1.54 cm² to 30 cm². He reported that the ulcers developed following surgery to repair an abdominal aneurysm.

After 2 years of standard wound care and many topical antimicrobial and oral antibiotic treatments, five lower extremity wounds remained in the lateral and medial aspect of the right lower leg as well as the medial aspect of the left lower leg. Before enrolling in this case study, the patient tried oral antibiotics on a recurring basis (ciprofloxacin in July 1998, November 1998, May 1999, June 1999, and August 1999; clarithromycin in June 1999 and August 1999). In addition, several different topical antimicrobials were tried, including mupirocin (Bactroban®, SmithKline Beecham Pharmaceuticals, Mississauga, Ontario, Canada), cadexomer iodine (Iodosorb®, Perstorp Pharma, Lund, Sweden), and nanocrystalline silver dressings (Acticoat®, Westaim Biomedical Corp, Exeter, NH, Fort Saskatchewan, Alberta, Canada) in combination with mechanical debridement. In general, the patient found it difficult to tolerate the application of topical antimicrobials because they exacerbated his pain.

At the time of this study, the patient’s wounds were superficial with no undermining and had attached edges and loosely adherent slough. Only minimal granulation tissue was present. Examination of the dressings showed that his wounds were producing copious amounts of purulent yellow exudate. Furthermore, significant erythema surrounded the wounds. Semiquantitative bacterial cultures obtained before treatment revealed the presence of three types of bacteria: methicillin-resistant S. aureus (MRSA) in his right medial lower ulcer and a combination of Pseudomonas aeruginosa and S. aureus in his left medial ulcer.

The wounds were treated with standard wound care consisting of saline cleansing, several layers of absorptive hydrofiber dressing (Acquacel®; Convatec, Skillman, NJ), mild compression therapy (Surepress®;Convatec, Skillman, NJ), and self-adherent tape (Coban®, 3M, St. Paul, Minn.).

Using the UVC treatment protocol described previously, the patient received seven UVC treatments over a 14-day period. Treatment was scheduled to coincide with dressing changes on alternate days. This intensive 2-week treatment period was followed by 1 month of weekly UVC treatments. Each wound received 180 seconds of UVC irradiation per treatment session. During the initial seven UVC treatments, the patient received no other antibiotic treatment. However, during the 1 month of weekly UVC treatments, the patient’s standard wound care regimen included a 15-day course of ciprofloxacin (500 mg bid) and a trial of sodium chloride-impregnated absorbent dressing (Mesalt®; SCA Molnycke, Regensdorf, Switzerland). Use of the sodium chloride-impregnated absorbent dressing was later discontinued because the subject reported he could not tolerate the increased pain that occurred when the dressing was applied.

The two wounds that were closely monitored were the left medial and right medial lower ulcer, which were approximately 18.3 cm² and 15.3 cm² in size, respectively. Results obtained from semiquantitative swabs taken from the two lower leg wound sites showed that heavy growth of P. aeruginosa (3+) was completely eradicated after the first UVC treatment and no growth of S. aureus was evident after 2 weeks of alternate day UVC treatments (see Figure 1). A continuing treatment program of one UVC treatment per week for 1 month, in addition to conventional wound care and antibiotics,
was required to remove MRSA from the wound bed. Of note: Both wounds contained a moderate growth (2+) of *S. aureus*.

In addition to marked changes in the type and relative amount of bacteria present within the wound bed, improvements in wound appearance were observed (see Figures 2a and 2b). After 1 month of UVC treatment, the authors observed the presence of epithelial buds, normal skin color surrounding the wound, and the emergence of healthy “beefy” red granulation tissue in the right medial lower wound. This improvement in wound appearance was reflected in a reduction of PSST scores (see Tables 1 and 2).

**Case 2**

A 78-year-old woman had poorly controlled type 2 diabetes for 12 years and lower extremity neuropathy for 5 years. She also had a decreased lower extremity blood flow (ABI < 0.8) and absent pedal pulses. Her medical history included: obesity, ischemic heart disease, atrial fibrillation, myocardial infarct, congestive heart failure, hypertension for 12 to 15 years, and poor pulmonary function, requiring intermittent use of oxygen administered via nasal prongs. She was admitted from a nursing home to the hospital for chronic pain and immobility, exacerbated by a history of spinal stenosis at L2, L3, and L5, with surgery in 1998, and osteoarthritis (OA) requiring left knee and bilateral hip replacements. She took numerous medications, including acetaminophen 500 mg, two tablets qid, for pain. Immobile for 3 months before admission, she had developed severe depression and anxiety that were poorly controlled. She presented at the hospital with an ulcer located on the fifth toe of her right foot that had been present for approximately 3 months before admission. A previous trial of oral antibiotics (levofloxacin, 500 mg OD for 7 days), was unsuccessful. Standard wound care consisting of saline cleansing and a transparent dressing (Tegaderm™, 3M, St. Paul, Minn.), in conjunction with wearing a protective boot, had not resulted in wound closure.

At the time of this study, the right fifth toe ulcer was approximately 0.4 cm². Semiquantitative swab cultures indicated that the toe ulcer was colonized with MRSA (see Figure 3). Before UVC treatment, the wound was superficial with no undermining, had attached edges, and contained loosely adherent slough, with minimal granulation tissue present. Examination of the wound dressings revealed that the wound was producing a moderate amount of serosanguineous exudate.

Using the UVC treatment regimen previously described, the patient was treated with seven consecutive, daily UVC treatments of 180 seconds each to the right fifth toe ulcer. During the UVC treatment period, she continued to receive the standard wound care described.

The reduction in bacterial bioburden of the ulcer (see Table 1) was associated with concurrent wound reepithelialization, and the ulcer was healed following 1 week of UVC treatments. This marked improvement in wound status was reflected in a change of PSST scores from a PSST score of 30 pre-UVC treatment to a score of 14 post-UVC treatment (see Table 2).
Case 3

Case 3 involves an 81-year-old man, with a medical history of Alzheimer’s Disease (5 years), dementia, falls, depression, and type 2 diabetes that was well controlled with diet. He had a history of developing recurring ulcers with infection on the plantar aspect of his toes, typically lasting months before healing. Contributing factors to the development of his toe pressure ulcers included: repeated pressure from walking more than 6 hours per day, biomechanical imbalances in the foot, loss of ankle muscle pump due to OA in the knees and previous right ankle triple arthrodesis, and bilateral lower extremity edema. The subject was receiving regular chiropody visits for wound debridement on the plantar surface of his feet.

At the time of this study, a painful blister on his left third toe had developed into an open, infected wound with purulent yellow drainage. The ulcer was superficial with no undermining, had attached edges, and contained nonadherent yellow slough. The wound was approximately 0.6 cm² in size (see Figure 4). Semiquantitative swab cultures indicated that the ulcer contained MRSA. The skin surrounding the ulcer was bright red, and his third toe was swollen. He had nonpitting edema extending >4 cm around the wound, with peripheral tissue induration between 2 cm and 4 cm extending less than 50% around the wound. The patient had undergone antibiotic therapy before treatment with UVC consisting of tetracycline (250 mg qid) for 10 days. However, antibiotic treatment in conjunction with standard wound care consisting of saline cleansing and dry gauze dressings was unsuccessful at achieving wound closure.

Using the UVC treatment protocol described, the patient was given daily, 180-second UVC treatments over a 7-day period. During the UVC treatment period, the patient continued to receive standard wound care and antibiotic therapy (tetracycline, 500 mg qid) for 10 days. The patient also was given vitamin E and acetaminophen.

Methicillin-resistant S. aureus in this wound as determined using semiquantitative swabs was reduced following a single treatment of UVC and remained low after 1 week of daily UVC treatments (see Table 1). Following completion of the 7-day daily UVC treatment, the ulcer was closed with complete wound reepithelialization. This improvement in wound status was reflected in a marked improvement in PSST scores (see Table 2).

Discussion

Research into alternative nonantibiotic modalities is necessary to combat the widespread emergence of antibiotic-resistant bacteria such as MRSA. Ultraviolet light C band with a wavelength of between 200 nm and 290 nm has been found to have bactericidal effects, particularly against antibiotic-resistant bacteria, as demonstrated in recent in vitro and in vivo experiments.24,26 This present case study examined the role of UVC in reducing wound bioburden and improving wound status in chronic, MRSA-infected ulcers. Results from this case study suggest that UVC treatment can
decrease the relative amount of MRSA. In all three cases, wound bioburden decreased, clinical signs of infection diminished, and the wound appearance improved as indicated by PSST scores. In Case 1, UVC treatment resulted in the progression towards wound closure as marked by improved epithelialization and the presence of distinct epithelial buds. In Cases 2 and 3, full wound closure was achieved, characterized by complete reepithelialization.

Two clinical studies examined the efficacy of ultraviolet light (UVL), which contains type A, B, and C wavelengths, in the treatment of chronic wounds. Wills et al. demonstrated in a randomized, controlled study that patients with superficial pressure ulcers, some of which were infected, healed faster when treated with UVL than control subjects receiving standardized wound care only. Nussbaum et al. found that a combined therapy of ultrasound and UVC with standardized wound care for individuals with pressure ulcers resulted in faster healing times than standardized wound care combined with laser. The present case study is the first clinical report to document the effects of a specific wavelength of UVC treatment on chronic ulcers infected with MRSA.

This case study suggests that previous findings by Conner-Kerr et al., indicating that UVC has bactericidal effects on MRSA when administered in vitro, can be applied to the clinical situation. The killing rates for MRSA for in vitro cultures were reported to be 99.9% at 5 seconds and 100% at 90 seconds. The authors found that a UVC treatment time of 180 seconds was required to produce similar bactericidal effects in chronic wounds. The optimal clinical treatment time and length of UVC required for a 100% killing rate of MRSA in human chronic infected wounds is still uncertain. Results presented in this case report suggest that although a single 180-second treatment of UVC can eliminate MRSA from chronic wounds initially colonized with light growth (1+) of MRSA, more UVC exposure given in subsequent UVC treatments was required for ulcers infected with heavy growth (3+) of MRSA. Furthermore, several UVC treatments given over a 1-month period were required to eliminate MRSA from wounds colonized with high levels of multiple types of bacteria.

Despite the presence of a low level of MRSA remaining in the wounds after the completion of UVC treatment, wound appearance markedly improved in all three cases and two subjects had complete wound closure. According to Dow et al., the presence of bacteria does not always indicate wound infection. In fact, bacterial infection in wounds is not only determined by the number of organisms present in a wound, but is also dependent on other factors, such as bacteria virulence and host resistance.

In Case 1, before and during UVC treatment, the wounds contained an antibiotic-resistant strain of S. aureus, MRSA; following UVC treatment protocol, these wounds had a moderate level (2+) of S. aureus. This apparent change in type of bacteria present in chronic wounds following UVC treatment has been observed previously by this research team and also has been reported by others (J. McCulloch, personal communication). The mechanism for this change in swab results from primarily MRSA to S. aureus is uncertain; however, it can be postulated that UVC has the ability to render MRSA more susceptible to oral antibiotics.

The semiquantitative swab is the preferred method
for bacterial determination in this case study because it is economically feasible and easily administered by staff. When the swabbing technique is compared with tissue biopsy, Levine et al. found a linear relationship between the swab and biopsy counts of viable bacteria in the same wound: 10^5 organisms by biopsy were equal to 10^6 organisms by swab culture. Herruzo-Cabrera et al. concluded in their study that when the semiquantitative swab approach was evaluated, the following were demonstrated: sensitivity of 97.8%, specificity of 86.9%, positive predictive value of 90.7%, and a negative predictive value of 96.8%. The researchers concluded that semiquantitative cultures are useful for surveillance of infection and equivalent to quantitative biopsy cultures.

The three patients described in this case report were on-and-off antibiotics numerous times. Two of these patients received oral antibiotics during the UVC treatments. The prescription of oral antibiotic therapy was left to the discretion of the individual’s attending physician (not the same individual in all three cases). As outlined in a recent article by Sibbald et al., oral antibiotics are not always indicated for chronic wounds with localized infection.

The frequency of UVC treatments administered varied for the individual cases presented in this report. The UVC protocol was changed based on a number of practical issues, including the frequency of dressing changes and proximity of the patient to the wound treatment center. The patients described in Case 2 and Case 3 were both residents of a local facility and received daily dressing changes. Therefore, it was feasible to administer daily UVC treatments. The patient presented in Case 1 was living at home some distance from the wound center, and wound dressings, including compression wraps, were changed less frequently. For this individual, the most feasible treatment protocol was UVC treatments given on alternate days over a 2-week period, followed by weekly UVC treatments for 1 month. The results showed that individuals who received more frequent UVC treatments required only 1 week of UVC treatments to achieve complete wound closure; whereas, the individual who had UVC treatments less often required more than 6 weeks of UVC treatment to eradicate MRSA from the wound bed.

The individual had a greater pretreatment bacterial bioburden with multiple types of bacteria, his ulcers were present for an extended duration of time, and he had multiple ulcers — all of which were much larger than those in either of the two other cases. Therefore, the authors are unable to assess the influence of different UVC treatment schedule on the results obtained in the present study.

**Limitations**

Concurrent wound care therapies, including the utilization of oral antibiotic therapy and wound dressing protocols, were not standardized in this study. Furthermore, the wound history, primary etiology of the wound, and medical history varied greatly between subjects and practical issues required the frequency of UVC treatments to be tailored to accommodate the patient and wound dressing protocol. The influence of these factors on the ability of UVC treatment to reduce MRSA colonization of chronic wounds cannot be assessed in this case series. An additional limitation of the present study is the extremely small sample size. Results obtained from these few individuals do not sufficiently represent the larger population of individuals with chronic wounds that are colonized with MRSA. Future work involving a larger sample size is warranted.

**Conclusion**

In this case study involving three patients with chronic wounds locally infected with MRSA in whom previous standard wound care and topical and oral antimicrobial therapy had failed, UVC treatment was found to reduce bacterial load and facilitate healing. This case study suggests that UVC is a promising adjunctive therapy for chronic wounds infected with antibiotic-resistant bacteria such as MRSA. However, only future randomized controlled trials can ascertain the efficacy of UVC and determine the optimal treatment dosage time and length of UVC treatment.

Additionally, prolonged and repeated exposures to ultraviolet light have been associated with an increased risk of developing certain skin cancers. Clinical use of ultraviolet light should be limited to specific indications such as MRSA-positive chronic wounds where other anti-microbial therapies have not been effective, are not available, or when their use is not practically feasible. Careful monitoring of UVC treatment effectiveness
using semiquantitative swab results is suggested and continued use of ultraviolet light after wound bioburden has been eliminated is not recommended. - ONM

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