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Prospective Investigation of Nasal Mupirocin, Hexachlorophene Body Wash, and Systemic Antibiotics for Prevention of Recurrent Community-Associated Methicillin-Resistant *Staphylococcus aureus* Infections

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Recurrent community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) skin infections are an increasingly common problem. However, there are no data on the efficacy of decolonization regimens. We prospectively evaluated 31 patients with recurrent CA-MRSA skin infections who received nasal mupirocin, topical hexachlorophene body wash, and an oral anti-MRSA antibiotic. The mean number of MRSA infections after the intervention decreased significantly from baseline (0.03 versus 0.84 infections/month, $P = <0.0001$). This regimen appears promising at preventing recurrent CA-MRSA infections.

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) skin infections are an increasingly common reason to seek medical care in clinics, urgent care centers, and emergency departments and appear to have driven up rates of visits to practitioners for skin infections (4, 9). Patients with CA-MRSA skin infections often report recurrent episodes, with recurrence rates reported from 12 to 58% (5–7, 11). Many experts suggest considering use of a decolonization regimen as a means to prevent recurrent MRSA infection in select situations (1, 5, 7, 14), despite no clinical data to support this approach (3, 7, 8).

From 22 August 2006 to 28 September 2009, we enrolled 31 adult outpatients recruited from a single infectious diseases private practice group in northern California. Patients were eligible if they were referred for management of recurrent MRSA infections and had ≥2 definite MRSA infections in the 6 months prior to enrollment, lacked active infection consistent with MRSA, and were not pregnant.

Enrolled patients were prescribed the decolonization regimen for a total of 10 days. The regimen included all of the following: nasal mupirocin (Bactroban Nasal; twice daily), topical 3% hexachlorophene body wash (Phisohex; daily), and an oral anti-MRSA antibiotic (trimethoprim-sulfamethoxazole [$n = 10$ patients], a doxycycline [$n = 15$ patients], or minocycline [$n = 6$ patients]). The choice of oral antibiotic was based on investigators choice and antibiotic susceptibility of prior MRSA isolates in a given patient.

Patients were interviewed in person at baseline and by phone at 2 weeks, 3 months, and 6 months by using a standardized questionnaire. The baseline survey, based on a previously developed instrument used for an epidemiologic investigation of MRSA (10, 11), asked about MRSA risk factors. Follow-up surveys asked about adverse drug effects at the week 2 interview and about incident skin and MRSA infections at all follow-up visits. Patient infections were considered either definite (microbiologic confirmation of CA-MRSA skin infection), probable (skin infection consistent with MRSA without microbiologic confirmation), or possible (skin condition that was inconsistent with MRSA skin infections). The study design was approved by the Institutional Review Board at Natividad Medical Center, and all subjects signed written informed consent. Data analysis was conducted using SAS version 9.1.3 (Cary, NC).

Among 31 patients enrolled, the mean age was 40 years (range, 18 to 80 years), 18 (58%) pateints were female, 14 (45%) patients were Caucasian, 10 (32%) patients were Hispanic, 2 (7%) patients were African-American, and 5 (16%) patients were of other ethnicity or did not provide information on race/ethnicity. Most (26/31, 84%) patients were healthy, with no major comorbidities, such as diabetes or a malignancy. Additional demographic, clinical, and risk factor data are shown in Table 1.

The median number of skin infections in the previous 6 months prior to enrollment was 3.0 infections per person (mean, 5.1 [SD, ±6.0]; range, 2 to 30). After receiving study medication, 81% patients reported completing the treatments as prescribed. The remaining 19% reported completing only part of the study treatment, and all noted not taking the systemic antibiotics but using the body wash and nasal mupirocin. Four of 31 (13%) patients reported mild gastrointestinal side effects. No other side effects were reported.

Mean length of follow up was 5.2 months; four patients were unable to follow up at various times during the study period. Of 31 patients, 5 patients (16%) had a definite or probable MRSA skin infection during the 6 month follow-up period. Of the 5 subjects who had an infection, 4 had a single infection and one patient had 3 infections. The mean infection rate in the month 6 follow-up period (0.03 infections per month) was lower than that in the 6-month period before the intervention (0.84 infections per month, $P = <0.0001$). When patients from the study analysis who did not follow up were removed, findings were still significant ($P = 0.0007$). Among those patients who developed an infection

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TABLE 1 Demographic, clinical, and MRSA risk factors of population[a]

Characteristic	% (no.) of patients				*P* value
	Total ($n = 31$)	No New MRSA skin infection ($n = 26$)	New MRSA skin infection ($n = 5$)	Relative risk (95% CI)	
Age in yrs, mean ± SD (range)	40 ± 16 (18–80)	39 ± 17 (22–80)	40 ± 17 (18–58)	1.0 (0.95-1.05)	0.94
Gender					
Male	42 (13)	35 (9)	80 (4)	Ref	
Female	58 (18)	65 (17)	20 (1)	5.5 (0.02–1.7)	0.13
Ethnicity					
Caucasian	45 (14)	46 (12)	40 (2)	Ref	
Hispanic	32 (10)	31 (8)	40 (2)	1.4 (0.24–8.3)	0.71
Other	23 (7)	23 (6)	20 (1)	1.0 (0.11–9.2)	0.99
Comorbidities					
Diabetes	6 (2)	8 (2)	0 (0)	–	0.99
Hypertension	16 (5)	19 (5)	0 (0)	–	0.56
Cancer	6 (2)	8 (2)	0 (0)	–	0.99
No. of previous skin infections in prior 6 months, mean ± SD (range)	5 ± 6 (2–30)	5 ± 6 (2–9)	4 ± 3 (2–30)	0.96 (0.79–1.2)	0.68
Other clinical/behavioral					
Complete (100%) adherence to decolonization regimen	81 (25)	77 (20)	100 (5)	–	0.55
Recent surgery	6 (2)	8 (2)	0 (0)	–	0.13
Recent hospitalization	36 (11)	42 (11)	0 (0)	–	0.99
Healthcare worker	19 (6)	19 (5)	20 (1)	0.95 (0.13-7.1)	0.99
Close contact of patient with recent skin infection	60 (18)	52 (13)	100 (5)	–	0.07
Homelessness	14 (4)	17 (4)	0 (0)	–	0.99
Drug use	10 (3)	12 (3)	0 (0)	–	0.99
Housing density, mean ± SD (range)	1.3 ± 1 (0.25–3)	1.4 ± 0.8 (0.25–3)	1.0 ± 0.3 (0.66–1.3)	0.50 (0.24–1.1)	0.07

[a] MRSA, methicillin-resistant *Staphylococcus aureus;* SD, standard deviation; Ref, reference group; recent surgery, patient reported undergoing surgery in the 12 months prior to enrollment; recent hospitalization, patient reported being hospitalized in the past 12 months prior to enrollment; close contact of patient with recent skin infection, someone that spends >20 h per week in the same space as the patient and had a skin infection in the past 6 months; homelessness, patient does not currently have a place to sleep or live; drug use, any illicit drug use in the past 12 months; housing density, number of people living in the patient's household divided by the number of bedrooms; –, unable to calculate due to zero cells.

during the follow-up period, the relapse of infection occurred at 27, 44, 51, 125, and 133 days after enrollment, respectively (the subject with 3 relapses had infections at 125, 188, and 198 days after enrollment). When comparing risk factors of patients with and without recurrent infections, we found no associations between MRSA risk factors and infection during the follow-up period (Table 1).

Our investigation is important, as to our knowledge it is the first to examine the efficacy of a decolonization regimen to prevent recurrent CA-MRSA infection (3, 8). We found that the regimens were relatively well tolerated and the reduction in infection rate from baseline was pronounced. Our results are consistent with an older clinical trial of monthly 5-day applications of mupirocin (without body cleaning) for prevention of methicillin-susceptible *Staphylococcus aureus* (MSSA), which found a mupirocin treatment decreased MSSA infection rates compared to placebo (12).

Our investigation has limitations. First, our investigation did not include a control group. Hence, we do not know if patients would have had a decrease in infections even if they didn't receive the topical and systemic antibiotics. Second, our duration of follow up was 6 months. The durability of the regimen at preventing recurrent CA-MRSA infections beyond this time frame is unclear. Third, our sample size was relatively small, and we were underpowered to perform important secondary analysis examining predictors of treatment failure. Fourth, our regimen is aggressive and included systemic antibiotics. Many experts recommend topical (including nasal) agents but do not routinely recommend systemic agents for decolonization (3, 7). It is possible that a less aggressive approach may have achieved similar results. Of note, our regimens did not include decolonization of other family members or environmental decontamination, which is sometimes recommended (2). We also did not recommend decolonization of household pets, such as dogs and cats, which has been used to break a cycle of recurrent infections (2, 13). Finally, we did not assess these regimens' abilities to decolonize patients, although we know in other populations mupirocin-based decolonization regimens usually eliminate colonization (12).

In summary, in a relatively small prospective uncontrolled investigation, we found that a combination of systemic and topical antimicrobial regimens was associated with a subsequent decrease in MRSA infections among those with recurrent CA-MRSA skin infection. Given the large scope of the problem of CA-MRSA skin infections and the sizeable minority of persons who suffer from recurrent infections, the regimen used in this study may be rea-

sonable to offer to patients who suffer from recurrent skin infections. However, due to limitations of our investigation, larger randomized controlled trials based on this regimen are warranted.

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