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Letters to the Editor

Frequency of High-Level Mupirocin-Resistant *Staphylococcus aureus* in a Tertiary Care Facility

Methicillin-resistant *Staphylococcus aureus* (MRSA) strains are frequently resistant to multiple antibiotics, antiseptics, and disinfectants (4). Therefore, the presence of MRSA, even as a mere colonizer, presents a serious threat, especially in hospitals and nursing homes (14). The Albuquerque Department of Veterans Affairs Medical Center (AVAMC) began using topical mupirocin to eliminate MRSA from the nares of all colonized individuals in 1991. This approach is considered safe and effective and lacks the morbidities, side effects, costs, and effects upon normal flora associated with oral antibiotics (1–3, 12, 13). However, several studies have appeared recently that associate mupirocin usage with the emergence of highly mupirocin-resistant MRSA (5–8, 10). To assess the impact of mupirocin usage at the AVAMC, the frequency and the level of mupirocin resistance were measured with 427 *S. aureus* isolates saved by the microbiology laboratory between 1989 and the first quarter of 1995 (Table 1). The collection included MSSA isolates cultured from invasive sites and all MRSA.

Methicillin and mupirocin resistances were measured in Mueller-Hinton agar by the agar dilution method (11) at twofold increments from 2 to 64 and 2 to 1,024 μg/ml, respectively. Isolates of *S. aureus* were considered methicillin resistant if the MIC was >2 μg/ml and mupirocin resistant if the MIC was 4 to 64 μg/ml (low-level resistance), 128 to 256 μg/ml (intermediate-level resistance), and ≥500 μg/ml (high-level resistance), respectively (7). Duplicate samples from the same patient were not included in the analysis unless a change in susceptibility occurred. Eighty-two percent (350 of 427) of the isolates were resistant to methicillin, 0.7% (3 of 427) were resistant to mupirocin but not methicillin, and 6.1% (26 of 427) were resistant to both methicillin and mupirocin. Mupirocin resistance was independent of the hospital unit or body site from which the isolate was collected.

S. aureus colonizes mucosa superficially, and very high local doses of mupirocin are achieved when mupirocin is applied as an ointment (20,000 μg/ml). Therefore, the clinical significance of low and intermediate levels of mupirocin resistance is questionable (7). However, four MRSA isolates, all collected between November 1994 and January 1995, displayed high-level resistance. These isolates originated from three patients in three separate units in the hospital who had been treated with mupirocin prior to the collection of the resistant isolate. In one patient, highly resistant isolates were recovered from both a urine culture and a tracheostomy site that had previously been colonized by mupirocin-susceptible MRSA. Approximately 3 weeks later, MRSA with high-level resistance to mupirocin was also isolated from the patient's nares.

TABLE 1. Frequency of mupirocin-resistant *S. aureus* from 1989 to 1995[a]

Yr	No. of mupirocin-susceptible and -resistant isolates				
	Susceptible	Low MIC	Intermediate MIC	High MIC	Total
1989–1990	93	7	0	0	100
1991	42	0	1	0	43
1992	72	2	0	0	74
1993	79	8	0	0	87
1994–1995	112	7	0	4	123
Total	398	24	1	4	427

[a] The difference between the 3.3 and 0% frequencies of high-level resistance in 1994 to 1995 and 1989 to 1994, respectively, was statistically significant by Fisher's exact test ($P = 0.016$), the Kruskal-Wallis test ($P = 0.04$), and the Exact JT test for trend overtime ($P = 0.06$).

Prevention of MRSA infections requires prompt treatment of critically ill patients and treatment and monitoring of carriers, particularly during outbreaks (14). However, high-level mupirocin resistance can be mediated by conjugative plasmids (9), and so the potential exists for the selection of widespread mupirocin resistance with increased use of mupirocin and a concomitant increase in treatment failure (7). The emergence of high-level mupirocin-resistant MRSA at the AVAMC since November 1994 further suggests that there is rapid selection for high-level mupirocin resistance once established. In this light, it may be prudent to limit the use of mupirocin to decolonizing patients with documented MRSA infections, individuals at high risk for developing systemic infections, and carriers associated with outbreaks.

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