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Topical Mupirocin for Eradication of MRSA Colonization With Mupirocin-Resistant Strains

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ABSTRACT

Topical mupirocin was able to interrupt colonization of 52% and 68% of methicillin-resistant *Staphylococcus aureus* (MRSA)-colonized patients carrying mupirocin-resistant and -sensitive strains, respectively, including 44.4% and 85.7% of those colonized only in the nares. Although a trend to decreased effectiveness was seen for clearing mupirocin-resistant MRSA, this agent can decolonize many patients with resistant strains (*Infect Control Hosp Epidemiol* 2001;22:578-580).

Colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) continues to be a major concern, and its ability to cause serious infections has prompted the search for an effective means of controlling carrier states. Mupirocin, a topical antibiotic, has been widely used for clearance of MRSA carriage during outbreaks.[1] However, extensive use of this agent has led to the rapid emergence of mupirocin-resistant strains.[2] Most resistance has been low-level (minimum inhibitory concentration [MIC] 4-256 µg/L), and since the concentration achievable in the nose is approximately 20,000 µg/L, it is probably of little or no clinical relevance.[3,4] However, outbreaks with high-level mupirocin resistance (MIC >256 µg/L) have been described.[2,5]

Our hospital, a 625-bed tertiary-care institution, experienced an increase in the number of MRSA-infected and -colonized patients in the latter half of the 1990s. Widespread use of mupirocin resulted in an increase in the prevalence of mupirocin-resistant strains.[2] The goal of this study was to determine the effect of this in vitro resistance on the ability of mupirocin to decolonize patients with MRSA.

METHODS

Study Design

Inpatients at the SMBD-Jewish General Hospital who are MRSA-positive on a nasal screen also have cultures obtained from wounds (if present), sputum (when possible), and urine (if catheterized). Inpatients found to be colonized with MRSA, between March 1994 and December 1998, were prospectively enrolled in this study. Patients were either uniquely nasal carriers, colonized in the nares and one or more other sites, or had MRSA isolated only from wounds, sputum, or urine.

Hospital Infection Control Measures

Patients colonized with MRSA were cohorted or placed in private isolation rooms and given antimicrobial soap baths (using 4% chlorhexidine gluconate) twice a week. Healthcare workers wore gowns and gloves to handle patients. Decolonization usually was attempted with topical mupirocin (2% mupirocin, formulated in an ethylene glycol base, provided as Bactroban, SmithKlineBeecham Pharmaceuticals, Philadelphia, PA).

Follow-up Specimens

Follow-up ("test of cure") cultures were done after a minimum of 72 hours' treatment (mean, 8 days; range, 2-49 days). These consisted of nasal swabs plus wound, sputum, or urine cultures if previously positive.

Microbiology

Kirby-Bauer susceptibility testing of all MRSA was performed with a 5-µg mupirocin disk (Oxoid Ltd, Basingstoke, England). An isolate was considered susceptible if a zone size of ≥14 mm was obtained.

Statistical Analysis

Differences in the proportion of cleared patients after use of mupirocin were analyzed using a two-sided Fisher's Exact Test for categorical variables.

RESULTS

A total of 71 patients were enrolled in the study. Mean age at enrollment was 78 (range, 36-93) years; 46 of the patients were male. Exclusive extranasal carriage of MRSA was detected in 20 subjects, and 51 were colonized in their nares. Twenty-six of the latter were strict nasal carriers, whereas 25 patients were also colonized in other sites: 18 (72%) in wounds, 28% in urine, and 20% in sputum.

At baseline, mupirocin-resistant strains were found in 38 (53.5%) of the 71 patients. Forty-eight patients were treated with mupirocin in addition to the usual infection control measures. Results for effectiveness of mupirocin in clearing MRSA are shown in the Table.

Overall, MRSA clearance occurred in 68% of treated patients colonized with a mupirocin-sensitive strain, compared with 52% of those harboring a mupirocin-resistant isolate (odds ratio [OR], 2.0; 95% confidence interval [CI_{95}], 0.5-8.0; P=.37). Clearance of MRSA in individuals colonized in multiple sites was achieved only in 56% and 33% of patients with mupirocin-sensitive and mupirocin-resistant strains, respectively (OR, 2.5; CI_{95}, 0.265-25.5; P=.64). Among patients colonized only in the nares, clearance of MRSA occurred in 85.7% and 44.4% of mupirocin-sensitive and mupirocin-resistant strains, respectively (OR, 7.5; CI_{95}, 0.45-252; P=.15).

DISCUSSION

Persistent staphylococcal carriage in patients with chronic skin conditions repeatedly treated with mupirocin has been interpreted as evidence of resistance to mupirocin being responsible for treatment failure.[6] However, it has been shown that the concentrations of mupirocin achieved in the nares exceed the MICs of even high-level–resistant mupirocin strains, and it can be argued that failure of treatment in those cases arose from factors other than resistance. To our knowledge, there are no previous clinical studies looking at effectiveness of mupirocin for eradication of mupirocin-resistant strains of MRSA.

We have shown previously that more than 70% of our institution's mupirocin-resistant isolates had a complete absence of growth inhibition around the mupirocin disk.[2] The zone of inhibition has been shown to correlate well with the MIC,[3] suggesting that these isolates possess high-level resistance, known to persist for prolonged periods of time, even after the selective pressure associated with mupirocin use is eliminated.[7]

The nasal clearance rates we achieved for the mupirocin-susceptible strains were comparable to those found in previous studies.[8,9] Our data show that, although there was a trend toward decreased effectiveness in clearing mupirocin-resistant strains, clearance occurred in a substantial proportion of patients harboring those resistant isolates, especially when colonization was restricted to the nares. However, the present study, with its small sample size, did not have the statistical power to detect a significant difference in clearance rates between the mupirocin-resistant and mupirocin-sensitive groups. For patients colonized in the nares only, a sample size of 54 patients would have been required for the observed difference in clearance rates (a difference of 40%) to reach statistical significance, with a power of 90%.

When colonization occurred in multiple sites, fewer patients showed clearance of MRSA, in both the mupirocin-sensitive and mupirocin-resistant groups. In such a population with multi-site colonization, reacquisition from wounds and other sites is probably more relevant than resistance to the agent, as has been suggested by Harbarth et al. [10]

The clearance rates of greater than 30% that we achieved, even with mupirocin-resistant strains, may be because we only included the first set of follow-up cultures done after treatment was started. In the literature, eradication is often defined as the absence of growth on cultures taken at weekly intervals for 3 weeks. However, for infection control purposes, our goal was to diminish colonization enough to decrease spread from patient to patient and not necessarily to achieve complete eradication. Furthermore, this study was to evaluate the clinical efficacy of mupirocin against mupirocin-resistant strains, by performing a point-prevalence comparison between mupirocin-sensitive and mupirocin-resistant groups, and not to assess whether mupirocin can successfully eradicate MRSA over time. Early studies evaluating mupirocin have shown that its effect is seen within 48 to 96 hours.[1,11]

TABLE
NUMBER OF SUBJECTS WITH METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*, BY SITE

	Nares Only	Nares Plus Other Sites	Total
Mupirocin-sensitive			
Total	11	12	33
Treated with mupirocin	7	9	25
Follow-up cultures done	7	9	22
Follow-up cultures negative	6	5	15
% clearance*	85.7	55.5	68
Mupirocin-resistant			
Total	15	13	38
Treated with mupirocin	9	9	23
Follow-up cultures done	9	9	23
Follow-up cultures negative	4	3	12
% clearance	44.4	33	52
P value†	.145	.637	.365

* Follow-up cultures negative/follow-up cultures done ×100.
† "Percent clearance" proportions between mupirocin-resistant and mupirocin-sensitive groups were tested for differences.

Our success in clearing MRSA also could be attributed to the higher doses of mupirocin our patients received. Although observational studies have suggested that 5-day treatments, with twice daily or thrice daily dosing, are more cost-effective and may be associated with similar eradication rates,[1,8,12] the practice in our institution is to apply mupirocin four times daily for 2 weeks, or until discharge.

We conclude that mupirocin is able to clear nasal MRSA carriage with mupirocin-resistant strains in approximately 50% of cases. A trend toward reduced effectiveness was observed when the strains are resistant to this agent, but our study did not have the statistical power to detect significant differences in clearance rates between the two groups. Thus, mupirocin still may be used with some success for nasal decolonization of mupirocin-resistant MRSA. A larger randomized and blinded study is needed to investigate this issue.

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