Frequency and Possible Infection Control Implications of Gastrointestinal Colonization with Methicillin-Resistant *Staphylococcus aureus*

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of health care-associated infections. Multiple factors, including transmission from unrecognized reservoirs of MRSA, are responsible for failure to control the spread of MRSA. We conducted prospective surveillance to determine the frequency of gastrointestinal colonization with MRSA among patients and its possible impact on nosocomial transmission of MRSA. Stool specimens submitted for *Clostridium difficile* toxin A/B assays were routinely inoculated on colistin-naladixic acid agar plates, and *S. aureus* was identified by using standard methods. Methicillin resistance was confirmed by growth on oxacillin-salt screening agar. For patients whose stool yielded MRSA, information regarding any previous cultures positive for MRSA or other organisms that would require contact precautions was obtained from the laboratory’s computer system. During a 1-year period, 151 (9.8%) of 1,543 patients who had one or more stool specimens screened had MRSA in their stool. Ninety-three (62%) of the 151 patients had no previous history of MRSA colonization or infection. Of these 93, 75 were inpatients. Sixty (80%) of the 75 inpatients with no previous history of MRSA were not under “contact precautions.” The 60 patients would have spent an estimated total of 267 days without being placed under contact precautions if their positive stool cultures had not resulted in their being isolated. Placing patients under contact precautions based on their positive stool cultures prevented an estimated 35 episodes of MRSA transmission. We conclude that gastrointestinal colonization with MRSA may serve as an unrecognized reservoir from which transmission of MRSA may occur in health care facilities.

Screening of patients at high risk of colonization by methicillin-resistant *Staphylococcus aureus* (MRSA) has been recommended as a measure for controlling transmission of the organism in health care settings (24). Culture of specimens from the anterior nares and other body sites, such as wounds from high-risk individuals, often identifies patients with unrecognized MRSA colonization (9, 12, 19, 38). Although gastrointestinal tract colonization by MRSA has been reported previously (4, 10, 29), culturing the stool specimens of patients who have been hospitalized for more than 3 days for potential pathogens is generally not recommended (33, 39). We conducted prospective surveillance of stool specimens in a hospital where MRSA is highly endemic to determine the frequency of MRSA gastrointestinal colonization among high-risk patients. A secondary aim of the study was to determine if recognition of gastrointestinal colonization by MRSA would affect the implementation of barrier precautions designed to reduce the spread of MRSA.

**MATERIALS AND METHODS**

As part of ongoing surveillance for MRSA in a 450-bed university-affiliated teaching hospital, all stool specimens submitted to the clinical microbiology laboratory for *Clostridium difficile* toxin A/B testing were inoculated onto colistin-naladixic acid (CNA) agar plates that were incubated under aerobic conditions at 36°C overnight. This approach was taken because it seemed likely that patients at risk of antibiotic-associated diarrhea due to *C. difficile* would also be at increased risk of carrying other resistant pathogens such as MRSA. Colonies growing on CNA agar with morphology characteristic of *S. aureus* were identified by using coagulase tests. Those identified as *S. aureus* were inoculated onto commercially available oxacillin-salt screening agar (BBL, Cockeysville, MD), and those capable of growing on oxacillin-salt screening agar were classified as MRSA. The number of colonies of MRSA growing on CNA plates was recorded as 1+ to 4+ , with 4+ representing a nearly pure culture of MRSA. One MRSA stool isolate was frozen for each patient.

When MRSA was recovered from a stool specimen, the clinical microbiology laboratory database, which includes data for at least the previous 8 years, was searched to see if the patient had any previous cultures positive for MRSA. If the patient had no previous cultures positive for MRSA, laboratory personnel notified the nursing unit where the patient was located so that the patient would be placed under “contact precautions,” as recommended by the Centers for Disease Control and Prevention (8).

For inpatients with no previous cultures positive for MRSA, a retrospective review was conducted to determine the ages and genders of affected patients and the extent to which isolation of MRSA from stool resulted in early placement of patients under contact precautions. The microbiology laboratory database was reviewed to determine if the patients had clinical cultures (e.g., of sputum, wound, or urine specimens) that yielded MRSA either before or after the stool culture was positive. For patients with a subsequent positive clinical culture, the number of days that patients would have been cared for without being under contact precautions (nonisolated days) was determined. If the patient’s gastrointestinal colonization with MRSA had not been detected by obtaining a culture of stool was calculated as follows: date of subsequent positive clinical culture – date of positive stool culture – number of nonisolated days prevented. For patients who did not have a subsequent clinical culture positive for MRSA during the same hospitalization, the following calculation was performed: date of discharge – date of positive stool culture – number of nonisolated days prevented. The total number of nonisolated days prevented was determined for the two groups of patients combined.

The number of transmissions of MRSA that may have been prevented by promptly placing patients under contact precautions following recovery of MRSA from their stool was estimated in the following manner. The number of
TABLE 1. Body sites from which specimens were taken for culture prior to MRSA-positive stool culture during current hospitalization

<table>
<thead>
<tr>
<th>Source of specimen for culture</th>
<th>No. (%) of patients with previous cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inpatients without known history of MRSA (n = 75)</td>
</tr>
<tr>
<td>Sputum</td>
<td>13 (17)</td>
</tr>
<tr>
<td>Urine</td>
<td>41 (55)</td>
</tr>
<tr>
<td>Wound</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Blood</td>
<td>42 (56)</td>
</tr>
<tr>
<td>Nares</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Other</td>
<td>20 (8)</td>
</tr>
<tr>
<td>None</td>
<td>18 (24)</td>
</tr>
</tbody>
</table>

* Six patients without previous cultures during the current hospitalization were positive for MRSA on previous admissions.

transmissions that may have occurred from patients under contact precautions that were instituted due to positive stool cultures (number of days in isolation × rate of transmission per day from patients in isolation [0.009 transmissions per day]) was subtracted from the number of transmissions that may have occurred if stool cultures had not resulted in institution of contact precautions (number of nonisolated days × the estimated risk of transmission per day of MRSA from patients not under contact precautions [0.14 transmissions/day]) (14).

RESULTS

During 2003, 1,543 patients had one or more stool specimens submitted to the clinical microbiology laboratory for C. difficile toxin A/B assays. A total of 159 (10%) patients had one or more stool specimens positive for C. difficile toxin A/B. Of the 1,543 patients who had stool specimens screened on CNA agar, 151 (9.8%) yielded MRSA. The average age of patients with MRSA was 74.7 years (range, 33 to 107), with 79.5% of affected patients being 65 years of age or older. Fifty-nine percent of patients with MRSA were female. Forty-six (30%) of the 151 patients had a stool culture positive for MRSA within the first three hospital days. For the remaining inpatients, the interval between admission and the stool culture positive for MRSA was 4 to 92 days (median, 8 days). The relative number of colonies of MRSA noted on CNA plates was 1+ for 11.3% of the 151 patients, 2+ for 25.2%, 3+ for 56.3%, and 4+ for 7.3%.

Ninety-three (62%) of the 151 patients had no previous cultures positive for MRSA, and for these 93 individuals, screening of stool cultures provided the first evidence that they were colonized with MRSA. Seventy-five of the 93 patients for whom stool cultures provided the first evidence of MRSA colonization were inpatients, while the remaining 18 were outpatients or were extended-care-facility residents who had stool cultures submitted to the clinical microbiology laboratory for processing. For the 75 inpatients, the body sites from which specimens were taken for culture before their MRSA-positive stool culture are shown in Table 1. Fifty-seven (76%) of the 75 inpatients had specimens taken for culture from one or more body sites during the current hospitalization prior to their MRSA-positive stool screening culture. Sixty (80%) of the 75 inpatients with newly recognized MRSA gastrointestinal colonization were not being cared for under contact precautions when the stool culture was performed. The remaining 15 affected inpatients were being cared for using contact precautions because they had other resistant organisms such as van-

FIG. 1. Prevalence of methicillin-resistant S. aureus in stool specimens submitted for C. difficile toxin assay, and frequency with which newly identified carriers were being cared for under contact precautions. C. diff, Clostridium difficile; Pts, patients; NH, nursing home.
care-associated MRSA (14, 37). Patients who have been identified as being at increased risk of MRSA colonization include those with a history of MRSA colonization or infection, hospitalization in the preceding year, residence in extended-care facilities, chronic skin lesions, or poor chronic health status (13, 19, 25, 38). The anterior nares are the most common site of *S. aureus* colonization and the site most frequently screened in order to detect colonized individuals. Advantages of screening the anterior nares include the ease of obtaining the cultures and the relatively high sensitivity of such cultures for identifying patients colonized with MRSA (31). Culturing of wounds or skin lesions in addition to the anterior nares increases the likelihood of detecting MRSA colonization (31, 38). Although the anterior nares are understandably considered the best single body site from which to take specimens for culture to screen patients for unrecognized MRSA colonization, rectal or gastrointestinal carriage occurs in a substantial proportion of patients with MRSA nasal colonization (4, 5, 10, 29, 40). We decided to conduct MRSA surveillance by screening stool specimens submitted to the laboratory for *C. difficile* toxin A/B assays for several reasons. Screening of a specimen already submitted to the laboratory for other purposes requires no extra nursing time to obtain a specimen for culture. Also, screening of stool specimens submitted for *C. difficile* toxin assays has been found to be a practical and simple method for identifying patients with unrecognized colonization by multidrug-resistant pathogens such as vancomycin-resistant enterococci (11, 15, 18). Furthermore, patients with gastrointestinal colonization by health care-associated pathogens (e.g., *C. difficile* or vancomycin-resistant enterococci) may serve as important sources of transmission, since they often contaminate adjacent environmental surfaces that may serve as a source from which health care workers contaminate their hands or gloves (2, 3, 6, 22, 26, 30).

We found that nearly 10% of patients who had stool specimens submitted for *C. difficile* toxin A/B tests had gastrointestinal tract colonization with MRSA. Importantly, our study found that more than half of the patients with gastrointestinal carriage had no history of MRSA colonization or infection and that 80% of the patients whose stool cultures yielded the first evidence of MRSA colonization were not being cared for using contact precautions. If stool cultures had not been performed for these patients, they would each have spent an average of 4 to 5 additional days without being cared for using appropriate barrier precautions. Transmission of MRSA from such nonisolated patients is estimated to occur nearly 15 times as frequently as from patients who are cared for using barrier precautions (14).

Our study has several limitations. Because of the manner in which surveillance cultures were performed, we did not establish the frequency with which nasal colonization with MRSA occurred in the population of patients surveyed. Therefore, we were not able to determine how the yield from performing stool cultures would have compared to culturing specimens from the anterior nares of patients. Quantitative cultures of stool from affected patients were not performed. Ray et al. found that 23 patients with both vancomycin-resistant enterococci and MRSA in their stool had an average of 4.7 log_{10} CFU of MRSA/g stool, and 25% of samples contained >6 log_{10} CFU/g stool (27). Recently, a small study of patients with antibiotic-associated diarrhea accompanied by heavy (3+ to 4+) MRSA growth in the stool found that patients had an average of 8 log_{10} CFU of MRSA/g stool (1). Since no cultures of environmental surfaces were performed as part of this surveillance strategy, we did not establish the extent to which patients with loose or liquid stools containing MRSA contaminate their immediate environment. Finally, our estimates of the impact of early placement of patients under contact precautions on potential transmission of MRSA to susceptible patients were based on published MRSA transmission rates rather than on prospective epidemiologic studies on the wards of affected patients. Such studies would have required periodic culturing of all other patients in nursing units housing colonized patients and molecular typing of all MRSA isolates.

In addition to identifying patients who may serve as sources of transmission of MRSA, screening of stool specimens from high-risk patients can identify those who may be at increased risk of developing MRSA infection. For example, Squier et al. found that patients in an intensive care unit or transplant unit who had both rectal and nasal carriage were significantly more likely to develop *S. aureus* infection than those with nasal carriage only (34). Furthermore, a number of investigators have reported that predominant growth of enterotoxin-producing strains of MRSA in the stool may have important consequences associated with development of enterocolitis or antibiotic-associated diarrhea (10, 16, 17, 20, 21, 23, 35, 36, 41). Despite these reports, MRSA has seldom been reported as a cause of enterocolitis or antibiotic-associated diarrhea in the United States (7, 28, 32). Recently, we reported 11 cases of antibiotic-associated diarrhea in patients whose stool specimens contained heavy growth of enterotoxin-producing strains of MRSA, with detectable amounts of staphylococcal enterotoxin in stool filtrates (1). Failure to identify common causes of nosocomial diarrhea suggested that MRSA was responsible for the patients’ diarrhea. Three of the 11 cases occurred during the first two months of 2003, when screening of cultures described in the present report revealed that a total of 25 patients had MRSA in their stool. These findings suggest that when patients develop nosocomial antibiotic-associated diarrhea that cannot be attributed to *C. difficile*, other enteric pathogens, or medications, culturing their stool for the presence of MRSA may be warranted to clarify the role that enterotoxin-producing strains of MRSA may play in causing antibiotic-associated diarrhea. However, it should be emphasized that recovery of MRSA from fecal specimens does not, by itself, warrant antibiotic therapy, since it represents colonization in a majority of patients.

In conclusion, in facilities where MRSA is endemic, screening of stool specimens submitted to the laboratory for *C. difficile* toxin assays for MRSA can detect patients with unrecognized gastrointestinal colonization with this multidrug-resistant pathogen. A substantial proportion of patients with gastrointestinal colonization who are identified in this manner have no history of colonization or infection with MRSA and are not being cared for using recommended barrier precautions. Such patients may serve as potential sources of transmission of the organism within the facility. Further studies are needed to determine whether or not detection of patients with gastrointestinal MRSA colonization has any greater effect on preventing transmission of the organism than screening of patients for nasal colonization.
REFERENCES


