Increase in the frequency of recovery of meticillin-resistant *Staphylococcus aureus* in acute and chronic maxillary sinusitis

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This study compared the rate of recovery of meticillin-resistant *Staphylococcus aureus* (MRSA) between the periods 2001–2003 and 2004–2006 in acute and chronic maxillary sinusitis. Cultures were obtained from 458 patients, 244 with acute and 214 with chronic maxillary sinusitis; 215 isolates were recovered in the 2 years between 2001 and 2003 (118 from acute and 97 from chronic sinusitis), and 243 in the 2 years between 2004 and 2006 (126 from acute and 117 from chronic sinusitis). *S. aureus* was isolated from ten (8 %) of the patients with acute sinusitis between 2001 and 2003, three (30 %) of which were MRSA, and from 13 (10 %) of the patients with acute sinusitis between 2004 and 2006, nine (69 %) of which were MRSA (*P*, 0.01). *S. aureus* was found in 15 (15 %) of the patients with chronic sinusitis between 2001 and 2003, four (27 %) of which were MRSA, and from 23 (20 %) of the patients with chronic sinusitis between 2004 and 2006, 14 (61 %) of which were MRSA (*P* < 0.05). Antimicrobial therapy was administered over the last 3 months to 122 (57 %) of the patients with chronic sinusitis. MRSA was isolated more often from these individuals (28/122; 23 %) than from those not treated previously (10/92 or 11 %) (*P* < 0.05). These data illustrate that a significant increase occurred in the rate of recovery of MRSA in patients with acute and chronic maxillary sinusitis over the periods studied.

**INTRODUCTION**

An increase in the recovery of meticillin-resistant *Staphylococcus aureus* (MRSA) was recently noted from various infectious sites of acute (Huang & Hung, 2006) and chronic (Manarey et al., 2004) sinusitis, as well as the nasal mucosa of normal individuals (Kuehnert et al., 2006). Here, we evaluated the changes in frequency of recovery of MRSA in acute and chronic maxillary sinusitis. The presence of MRSA in the infected sinus may not only lead to failure of antimicrobial therapy, but may also serve as a potential source for the spread of these organisms to other body sites, as well as an origin for dissemination to other individuals. Furthermore, MRSA that also produces β-lactamase can survive treatment with β-lactam antibiotics and continue to protect penicillin-susceptible pathogens from penicillins (Brook & Foote, 2006).

This study compared the rate of recovery of MRSA between the periods 2001–2003 and 2004–2006 in acute and chronic maxillary sinusitis in adults.

**METHODS**

**Patients and symptoms.** The population studied was middle class, residing in suburban locations in the vicinity of Washington, DC, USA. The patients were seen consecutively in the outpatient clinic between 1 January 2001 and 1 January 2007 and were diagnosed as suffering from acute or chronic bacterial maxillary sinusitis.

Patients with acute infection had symptoms lasting between 10 and 30 days, whilst those with chronic infection had symptoms for over 90 days. None of those with acute sinusitis had received antimicrobial therapy during the last 2 months or had contact with hospitalized patients. None of those with chronic sinusitis had had previous sinus surgery.

Patients’ complaints included facial pain, frontal headache, purulent nasal discharge, fever and malaise. Occipitomental (Waters’ view), lateral, oblique and verticomental views or computed tomography scans were obtained. Sinusitis was defined radiographically as complete sinus opacity, an air-fluid level or mucous membrane thickening of at least 6 mm in the maxillary sinus. For the Waters’ view, mucosal thickening of the maxillary sinuses was measured as the shortest distance from the air–mucosal interface to the most lateral part of the maxillary sinus wall. Specimens were obtained by endoscopy and the sinus secretions were collected with calcium alginate-tipped micro-swabs. The study was granted institutional review board approval.

**Abbreviation:** MRSA, meticillin-resistant *Staphylococcus aureus*.
Cultures. Cultures were obtained using endoscopic aspiration before therapy using calcium alginate-tipped swabs, which were immediately plated into medium supportive of the growth of aerobic and anaerobic bacteria. The methods of specimen collection and microbiological evaluation have been described previously (Brook et al., 1996). Specimens were processed semi-quantitatively and organisms were identified using standard methods (Murray et al., 2003).

Antibiotic screening. S. aureus isolates were screened for oxacillin resistance using the Clinical and Laboratory Standards Institute (formerly the National Committee for Clinical Laboratory Standards) disc diffusion method (NCCLS, 2003). Overnight cultures from blood agar plates were suspended in Mueller–Hinton broth to the turbidity of a 0.5 McFarland standard, plated on Mueller–Hinton agar and a 1 μg oxacillin disc was placed onto the inoculum. Zone diameters were measured and recorded after 24 h incubation at 35 °C and susceptibility/resistance was recorded as follows: susceptible, equal or greater than 13 mm diameter; intermediate, 11–12 mm diameter; resistant, equal to or less than 10 mm diameter. MRSA strains were not typed.

Statistical analysis. Statistical significance was calculated using an unadjusted Fisher’s exact test (two-sided).

RESULTS
A total of 458 patients, 244 with acute and 214 with chronic maxillary sinusitis, were studied; 215 isolates were recovered in the 2 years between 2001 and 2003 (118 with acute and 97 with chronic sinusitis), and 243 in the 2 years between 2004 and 2006 (126 with acute and 117 with chronic sinusitis). Their ages ranged from 18 to 75 years, and 259 (57%) were male. No differences were noted in the age distribution, ethnicity or gender of the patients in the two study periods.

S. aureus was isolated from ten (8%) of the patients with acute sinusitis between 2001 and 2003 (as the only isolate in seven instances), and three (30%) of these isolates were MRSA. S. aureus was recovered from 13 (10%) of the patients with acute sinusitis between 2004 and 2006 (as the only isolate in nine instances), and nine (69%) of these isolates were MRSA (P <0.01) (Table 1). S. aureus was found in 15 (15%) of the patients with chronic sinusitis between 2001 and 2003 (as the only isolate in five instances), and four (27%) of these isolates were MRSA. S. aureus was recovered from 23 (20%) of the patients with chronic sinusitis between 2004 and 2006 (as the only isolate in seven instances), and 14 (61%) of these isolates were MRSA (P <0.05) (Table 1). Antimicrobial therapy was administered over the last 3 months to 122 (57%) of the patients with chronic sinusitis. MRSA was isolated more often from these individuals (28/122; 23%) than from those not treated previously (10/92; 11%). (P <0.05). The antimicrobials administered to the 38 patients with chronic sinusitis from whom MRSA was isolated were fluoroquinolones (15 patients), extended-spectrum macrolides (12 patients), cephalosporins (six patients) and amoxicillin/clavulanate (five patients).

Table 1. Recovery of S. aureus from 244 patients with acute and 214 with chronic maxillary sinusitis between 2001 and 2003 and between 2004 and 2006

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<tr>
<td></td>
<td>Meticillin-sensitive (%)*</td>
<td>Meticillin-resistant (%)*</td>
</tr>
<tr>
<td>2001–2003</td>
<td>7 (70)</td>
<td>3 (30)</td>
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<tr>
<td>2004–2006</td>
<td>4 (31)</td>
<td>9 (69)‡</td>
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*Percentage of isolates recovered from patients with this condition.
†Percentage of patients.
‡P <0.01 compared with the rate in 2001–2003.
§P <0.05 compared with the rate in 2001–2003.

DISCUSSION

These data illustrate that a significant increase occurred in the rate of recovery of MRSA in patients with acute and chronic maxillary sinusitis. These findings are in concordance with the overall increased recovery of MRSA from various other respiratory and non-respiratory tract infections (Lodise & McKinnon, 2007). These findings support the growing evidence that the burden of health-care-associated MRSA disease in the USA is high and may be increasing. In a multi-regional survey of MRSA disease, investigators from the Centers for Disease Control and Prevention observed significant increases in both community- and health-care-associated infections at several sites when comparing data from 2001–2002 with data from 2004–2005 (Klevens et al., 2007).

The association between previous use of antimicrobial therapy and increased isolation of MRSA has been noticed in the community and in other infections (Boyce, 2002; Schneider-Lindner et al., 2007) as well as in patients with sinusitis (Boyce, 2002). Similar to the observation by
Gerencer (2005), we also found that the majority of patients with chronic sinusitis infected with MRSA who were treated previously with antimicrobials had been treated with either a fluoroquinolone or an extended-spectrum macrolide antibiotic. As almost all strains of MRSA are resistant to these agents, it is possible that these classes of antibiotics may be creating an environment within the sinuses that is particularly conducive for MRSA growth.

Treatment of sinus infection associated with the recovery of MRSA is challenging. It is important to provide coverage against these organisms as well as against other potential aerobic and anaerobic pathogens. Although vancomycin represents the gold standard for therapy of MRSA infections, reports of increasing in vitro resistance to vancomycin (Howden et al., 2006), combined with reports of clinical failures (with this and other anti-staphylococcal agents), underline the need for alternative therapies. Older agents with favourable in vitro activity available in both oral and intravenous dose forms include trimethoprim/sulfamethoxazole and clindamycin. Limited clinical data exist to support their routine use as initial therapy in the treatment of MRSA infections. However, these and other options (e.g. tetracyclines) are being re-explored in the setting of increasing concern over MRSA acquired in the community setting. Newer treatment options of therapies for MRSA include linezolid, quinupristin/dalfopristin, daptomycin and tigecycline.

Culture-directed oral and topical antibiotic therapy has been utilized effectively in the treatment of MRSA sinusitis (Gerencer, 2005). Even though the gold standard of obtaining such a culture is through a surgical specimen or punctures (Anon et al., 2004), cultures obtained through nasal endoscopy have been shown repeatedly to provide adequate culture results (Benninger et al., 2006). The topical antibiotics included gentamicin, tobramycin, vancomycin, ciprofloxacin and mupirocin. Topical application of antibiotics to the sinus membranes offers the potential benefit of a high concentration of the drug at the site of infection.

Further prospective studies and continuous monitoring of the rate of recovery of MRSA in acute and chronic sinusitis are indicated. The results of our study, which demonstrate the increased role of MRSA in sinusitis, underline the importance of performing routine endoscopic cultures, especially in patients who fail to respond to empirical antimicrobial therapy.

Conclusions

A comparison of the rates of recovery of MRSA between the periods 2001–2003 and 2004–2006 in acute and chronic maxillary sinusitis illustrated a significant increase in the rate of recovery of this organism in patients with acute and chronic maxillary sinusitis. These findings suggest the use of an increased index of suspicion for the presence of MRSA in sinusitis and greater use of sinus cultures, especially in patients who do not improve or who fail to respond to antimicrobial treatment after 48 h of therapy, to guide the proper selection of antimicrobial agents.

REFERENCES


