Methicillin-resistant Staphylococcus aureus preventing strategy in cardiac surgery

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Abstract

Objectives: The aim of this survey was to elucidate the efficacy of methicillin-resistant Staphylococcus aureus (MRSA) preventing strategy in our institution by investigating the incidence and evaluating the morbidity and mortality associated with this multi-resistant virulent organism. Methods: A prospective observational cohort among patients submitted to cardiovascular surgical procedures was conducted from 1 January 1997 to 31 December 2005. Preventing strategy included active screening programs by nasal swabs for all patients admitted from other hospitals or at risk for developing infectious complications. Carriers or infected patients remained isolated and were treated promptly. Furthermore, all newly employed health care workers were screened for MRSA and carriers were treated with mupirocin until the eradication of the pathogen. Results: Throughout the 9-year study period 826 infectious complications were registered among 15,270 cardiac surgical patients. Total infection rate was 5.4%. MRSA was identified in 86 patients; 56 patients proved carriers and 30 infected. The MRSA associated infection rate was 0.2%. During this period of time mean ICU stay was 1.7 days and ICU mortality rate was 2.9%. MRSA infected patients presented a mean ICU stay of 46.5 days and a mortality rate of 30%. In ten patients, MRSA was detected in tracheal secretions, in four patients in swabs taken from donor site infection and in four patients from superficial sternal surgical wound. In ten patients the pathogen was isolated from cultures of the surgical site drainage and the diagnosis of post-sternotomy mediastinitis was confirmed. The remaining two patients were defined as having severe sepsis; MRSA was documented in central venous catheter tips and blood cultures. Conclusions: The prompt determination, isolation and appropriate treatment of MRSA patients admitted from other institutions combined with the detection and elimination of carriers among new health care workers and patients at high risk of developing infectious complications prevented further spread of the pathogen.

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Keywords: MRSA; Preventing strategy; Cardiac surgery

1. Introduction

The emergence of antibiotic resistant strains of Staphylococcus with the capacity to produce outbreaks of infections among hospital patients is a relatively old problem of universal concern. In the early 1980s the prevalence of penicillin resistance in intensive care units (ICU) and surgical settings exceeded 85% [1] owing to the development of bacterial defense mechanisms. Considerable variations in the isolation of methicillin-resistant Staphylococcus aureus (MRSA) have been reported between institutions and geographic areas [2, 3]. In Greece, MRSA prevalence remains extremely high accounting for 11.1–90.0% of S. aureus isolates in ICUs and 12.5–83.3% in surgical wards. Evidence from controlled studies reveals that invasive MRSA infection is associated with significant increase in mortality, prolonged hospital care and substantial extra costs [4, 5]. The adverse prognosis associated with MRSA bacteremia and deep surgical site infection appears related in part to suboptimal efficacy of therapy with glycopeptides and to the underestimation of cross infection from patient or health care worker to patient. Elimination of MRSA reservoir in hospitals has been reported effective [6]. In our institution prophylactic measures include the mandatory screening of recently employed health care workers and active screening programs for patients admitted from other hospitals. Prompt isolation and appropriate treatment of MRSA infected patients is also implemented. The aim of this study was to elucidate the efficacy of the above preventing strategy in patients undergoing cardiac surgery by investigating the incidence and evaluating the morbidity and mortality associated with this multi-resistant virulent organism.

2. Material and methods

The study was designed as a prospective observational cohort of critically ill patients with ICU-acquired infections caused by MRSA strains. The survey was conducted at the 16-bed Surgical ICU (SICU) of Onassis Cardiac Surgery Center (OCS) in Athens among 15,270 patients admitted to cardiovascular procedures and attended at the SICU in
accompanying with their clinical evolution. From 1 January 1997 to 31 December 2005 MRSA patients were identified through the electronic databases for antibiotic use and in vitro antimicrobial susceptibility results. All case histories of the patients were subjected to meticulous analysis.

Throughout the 9-year study period routine nasal swabs were obtained from all patients admitted from other hospitals or being repeatedly hospitalized. As a general policy, patients at risk for MRSA remained isolated for 48 h and were transferred to an ordinary ward when they proved MRSA negative. Carriers or MRSA infected patients were treated promptly. Furthermore, most surgeons recommended the pre-operative screening of their patients with swab cultures of the anterior nares and initiated the subsequent preoperative de-colonization with nasal 2% mupirocin after MRSA identification. Barrier precautions, similar to the Centers for Disease Control guidelines [7] for contact precautions, were used in each MRSA positive patient. In brief, these measures consisted in flagging microbiological reports, charts and doors of MRSA positive patients and wearing gloves and gowns when entering the room and caring for the patient. Hand washing with antiseptic soap or alcohol-based hand rub solution after contact with the patient was implemented. Solution is placed in wall-mounted dispensers at the entrance of each room. In addition, all new health care workers were also screened for MRSA and nasal carriers were treated with mupirocin until the eradication of the pathogen was confirmed.

Prospective data were collected on all patients submitted to open heart surgery. The same group of surgeons, with minor changes during the 9-year study period, performed all operations. The same team of anesthesiologists according to a standard protocol provided anesthetic management. At the induction of anesthesia all patients submitted to coronary artery by-pass grafting (CABG) received cefuroxime intravenously as a single dose (3 g), while in patients who underwent valvular replacement a combination of two doses of 400 mg teicoplanin and three doses of 2 g ceftazidime for 24 h was administered.

A surgeon independent group examined all patients for the development of infectious complications. Chest X-rays and laboratory tests were performed in a routine base. In case of suspected infection cultures of blood, urine, central venous catheter tips and tracheal secretions were taken. If any wound secretion was observed, swabs were obtained for bacteriological examination and were plated on an agar plate not supplemented with oxacillin and incubated for 48 h at 37 °C. S. aureus was identified as Gram-positive cocci producing free coagulase. Minimum inhibition concentration (MIC) of oxacillin, erythromycin, clindamycin and quinupristin/dalfopristin was determined by E-test (Biodisk, Solna, Sweden) and the results were interpreted as recommended by the Greek Society for Microbiology.

For experimental reasons, total DNA was extracted from seven MRSA isolates expressing additional resistance to macrolides–lincosamides and PCR was carried out. The presence of mecA, ermA(A), ermA(B), ermC and msrA/msrB resistant genes was identified by agarose gel electrophoresis of PCR products and verified by hybridization of Clal DNA digests with the specific mecA and ermA(A) probes and the Tn554 transposon. Clones of MRSA were defined by the combination of Clal-mecA types Clal-Tn554 polymorphisms and Pulsed-Field Gel Electrophoresis (PFGE) patterns.

Data variables extracted for evaluation included surgical procedure, nature of complication, pre-existing medical conditions and co-morbidities (diabetes mellitus, chronic obstructive pulmonary disease, etc.), presence of prosthetic material and intra-vascular devices and outcome (mortality, length of hospital stay). Additional data regarding infectious complications were also collected including positive bacterial cultures, antibiotic susceptibilities, antibiotics administered, dates and sites of the first bacterial isolation, subsequent cultures results, the duration of therapy and infection related outcome.

Diagnosis of pneumonia required the presence of new, persistent and otherwise unexplained pulmonary infiltrates appearing on the chest radiograms. Moreover, at least two of the following criteria were also mandatory: (i) temperature of >38 °C; (ii) leucocytosis of >10,000 cells/mm³ or leucopenia; and (iii) purulent respiratory secretions. Tracheobronchial secretions and/or bronchoalveolar lavage (BAL) specimens were used for microbiological diagnosis of pneumonia using non-quantitative cultures. Other infections, such as urinary tract infections and central venous catheter-related infections, were defined based on the guidelines issued by the Centers for Disease Control and Prevention. If bacteraemia was suspected, at least two blood samples were obtained for culture from separate sites before the initiation of therapy. Septic shock was defined as sepsis with prolonged hypotension despite adequate fluid resuscitation, together with the presence of perfusion abnormalities such as oliguria or acute alteration in mental status.

Clinical cure was defined as resolution of presenting symptoms and signs of infection by the end of antibiotic treatment, while clinical improvement as partial resolution of these signs. Clinical failure was defined as persistence or deterioration of presenting symptoms and/or signs of infection during antibiotic administration (unresponsiveness) and recurrence of infection as the occurrence of a new episode of infection at least 72 h after clinical resolution of a preceding episode. Eradication of the pathogen was defined as absence of growth in the final culture of clinical material and intra-vascular devices and outcome.

Infections are daily registered by an Infection Control Nurse (ICN) and twice monthly discussed at the Infection Control Committee (ICC). All surgical patients are examined in the outpatient clinic 30 days after hospital discharge and the registration of post-hospitalization infections is ensured. Infections are independently reported to the ICC by the outpatient nurse and the surgeon and selectively by the ICN. The Institutional Review Board approved the study, but since only routine clinical and laboratory examinations were evaluated no Ethical Committee approval was necessary.
3. Results

Throughout the 9-year study period, 826 infectious complications were registered among 15,270 cardiac surgical patients. Total infection rate was 5.4%. MRSA was identified in 86 patients; 56 patients proved carriers and 30 infected. The MRSA associated infection rate was 0.2%. During this period of time mean ICU stay was 1.7 days and ICU mortality rate was 2.9%. MRSA infected patients presented a mean ICU stay of 46.5 days and a mortality rate of 30%. Twenty MRSA carriers were detected during pre-operative screening with swab cultures of the anterior nares. Subsequent decolonization with nasal 2% mupirocin after MRSA identification was initiated until the eradication of the pathogen was confirmed.

All cases of MRSA infections were isolated after the cardiovascular surgical procedure. In ten patients MRSA was detected in tracheal secretions, in four patients in swabs taken from donor site infection and in four patients from superficial sternal surgical wound. In ten patients the pathogen was isolated from cultures of the surgical site drainage and the diagnosis of post-sternotomy mediastinitis was confirmed. The remaining two patients were defined as having severe sepsis; MRSA was documented in central venous catheter tips and blood cultures. Meticulous examination of seven MRSA isolates for the detection of resistant genes revealed that five pathogens carrying the \(\text{erm}(C)\) gene belonged to the multi-resistant clones – III’::KK::B and X’::KK::B widely distributed among strains of Greek hospitals. In addition, two MRSA isolates presented the \(\text{erm}(A)\) gene and belonged to different clones. Results are summarized in Table 1.

Further investigation revealed that risk factors for MRSA infection and bacteremia were prior hospitalization (n: 6), re-sternotomy (n: 9), longer by-pass and aortic cross-clamp time (n: 19), postoperative heart failure and use of intra-aortic balloon pumping (IABP) (n: 9), postoperative renal failure (n: 13), combined CABG with valve or aortic surgery (n: 12) and re-operation for bleeding (n: 9). Table 2 depicts the demographic and clinical characteristics of MRSA infected patients included in the study.

All patients received a combination of vancomycin or teicoplanin or linezolid with rifampin or aminoglycoside. Clinical cure or improvement was observed in 21 patients treated with vancomycin or linezolid with rifampin or aminoglycoside. All patients received a combination of vancomycin or linezolid with rifampin or aminoglycoside. Clinical cure or improvement was observed in 21 patients treated with vancomycin or linezolid with rifampin or aminoglycoside. All patients received a combination of vancomycin or linezolid with rifampin or aminoglycoside. Clinical cure or improvement was observed in 21 patients treated with vancomycin or linezolid with rifampin or aminoglycoside. All patients received a combination of vancomycin or linezolid with rifampin or aminoglycoside. Clinical cure or improvement was observed in 21 patients treated with vancomycin or linezolid with rifampin or aminoglycoside. 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Table 1

<table>
<thead>
<tr>
<th>Infections (1997–2005) in the cardiac SICU</th>
<th>n</th>
<th>Gram (+)</th>
<th>Gram (-)</th>
<th>MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract infection</td>
<td>86</td>
<td>45</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>Pulmonary tract infection</td>
<td>218</td>
<td>118</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>Superficial surgical site infection</td>
<td>14</td>
<td>8</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Deep surgical site infection</td>
<td>220</td>
<td>119</td>
<td>101</td>
<td>10</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>29</td>
<td>16</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Bacteremia-sepsis</td>
<td>259</td>
<td>140</td>
<td>119</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>826</td>
<td>446</td>
<td>380</td>
<td>30</td>
</tr>
</tbody>
</table>

SICU (no patient died in the ward following ICU discharge). Eradication of the pathogen was observed in 21 cases. Patients with signs of mediastinitis due to MRSA were treated by debridement, radical removal of infected tissue and in one case the addition of an omentum flap. In all cases a closed continuous irrigation with saline/vancomycin was installed after direct primary closure of the sternum in accordance with patient’s clinical evolution. The clinical outcome of post-sternotomy mediastinitis was poor despite prompt therapeutic interventions. MRSA mediastinitis mortality rate was 30% (n: 3).

4. Discussion

Staphylococcus aureus, a bacterium found commonly on skin, has acquired increasing resistance to a wide range of antibiotics. Over the past three decades MRSA has spread in hospitals worldwide, becoming endemic in many countries [8, 9]. In a recent survey of 3051 S. aureus isolates from 25 University hospitals (participating in the SENTRY study) distributed among 15 countries of Central and Southern Europe, MRSA strains constituted 25% of all isolates; the highest prevalence was observed in hospitals in Portugal (54%) and Italy (43–58%), whereas the lowest prevalence was detected in institutions in Switzerland and The Netherlands (2%). Moreover, in Scandinavia MRSA prevalence is reported < 1% [3]. This variability might be due to geographic variations of MRSA strains with different virulence or colonization properties, or it reflects differences in the use of antibiotics and in hospital infection control policies. In Greece, according to data confirmed by the Greek System for Surveillance of Antimicrobial Resistance, mean MRSA prevalence translated to bacterial isolates among all clinical specimens varies from 35.5% in medical wards to 44.8% in surgical wards and 63.4% in ICU settings.

S. aureus possesses an impressive array of adhesins, exotoxins and other virulence factors that account for its capacity of causing invasive disease. The appearance of oxacillin-resistant S. aureus is attributed to mecA gene, the genetic determinant necessary for the expression of resistance to multiple antimicrobial agents [10]. Furthermore, a highly vancomycin-resistant MRSA strain, which had...
acquired the enterococcal van gene, has been described in
the USA [11]. Persistent or prolonged MRSA bacteremia
unresponsive to vancomycin therapy has led to the treat-
ment of these infections with other agents, as quinupristin,
dalfopristin, linezolid or daptomycin [12].
Molecular epidemiological studies indicate that the mas-
se geographic spread of MRSA results from the dis-
semination of relatively few epidemic clones [13]. Skin and soft
tissue infections, like furunculosis, cellulitis or abscess are
the most frequent and are characterized by the best clinical
outcome. In our study, eight patients presented with donor
or superficial surgical site infection. All of them recovered
successfully. On the other hand, deep sternal wound infec-
tion is an infrequent, yet potentially devastating compli-
cation following CABG or valve replacement [14]. The
reported incidence of post-sternotomy mediastinitis ranges
between 1% and 3% and the relevant in-hospital mortality
reaches 20% [15, 16]. Furthermore, prosthetic cardiac
valves may be infected with MRSA causing endocarditis,
perivalvular abscess and bacteremia [12] or disseminated
intravascular coagulation (DIC) and MOF [17]. Recent in-
vestigations identify that panton-valentine leukocidin (PVL)
positive infections are responsible for severe necrotizing
pneumonia with significant lethality (75%). In our institu-
tion, MRSA was detected in tracheal secretions of ten
patients and in swabs taken from deep surgical site infec-
tion of another 10 (0.07%) patients. MRSA mediastinitis
mortality rate was 30% (n: 3).

MRSA prevalence rates are significantly higher in critical
care vs. other hospital care sectors. Risk factors for acqui-
sition of healthcare associated MRSA include the prior stay
in hospital or chronic care facility, the extensive use of
broad-spectrum antibiotics, the exposure to invasive
devices and procedures [18, 19], the co-existence of skin
diseases or surgical trauma, co-morbidities like serious
neoplastic or metabolic diseases, the contact with non-
isolated MRSA carriers and the prolonged stay in an inten-
care or burn unit. The direct economic cost of MRSA
bacteremia in the European Union is conservatively esti-
mated at €117 million annually, while the total burden of
MRSA infections in Europe is summarized in 11,697 cases of
bacteremia and 1277 attributable deaths.

The implementation of hospital infection control mea-
urses, including patient screening, on-site surveillance,
contact isolation, a computerized alert system, and hospi-
tal-wide promotion of hand hygiene in association with the
improved ward and theatre hygiene, has been documented
to decrease the incidence of MRSA. An eight-year cohort
study of 1771 MRSA-positive patients evaluated the conse-
quences of delayed containment of a hospital-wide out-
break of MRSA infection during a four-year absence of
infection control procedures. An increase in the rate of
new MRSA infected or colonized patients was observed in
the first five years of the study period and subsequently
decreased after implementation of the appropriate infec-
tion control measures [20]. Specific recommendations
regarding the optimal methods to prevent MRSA infections
in surgical patients are difficult to provide, due to limited
scientific evidence and variable hospital MRSA rates.

Some investigators suggested that routine admission
screening cultures substantially benefited MRSA control in
endemic settings by promptly identifying the entire reser-
voir of MRSA [21]. In addition, weekly screening increased
both the rate and the promptness of MRSA detection,
allowing earlier institution of contact precautions [22].
Recent surveys also advocate screening at admission and
during hospital stay in high-risk patients or units [23].
Furthermore, in hospitals with endemic MRSA the pre-
operative screening of all patients with swab cultures of
the anterior nares and all open wounds has been recom-
med. If MRSA is identified on screening, then pre-
operative elimination of the pathogen with nasal 2%
mupirocin can be initiated. If follow-up cultures reveal
persistent MRSA colonization, then the use of vancomycin
for peri-operative antibiotic prophylaxis is mandatory.

Since the opening of the OCSC in 1993 an enhanced,
targeted infection control program included the obligator-
y isolation of all patients admitted from other hospitals, their
screening for MRSA and the eradication of the pathogen in
colonized patients. Carriers, MRSA infected or patients who
become positive during their hospital stay remain isolated
and are treated with the suitable antimicrobial combina-
tion. Furthermore, new health-care workers are screened
for MRSA and carriers are treated with nasal 2% mupirocin
until the verification of their de-colonization, as the prin-
cipal mode of MRSA transmission is transfer of the organism
from a carrier or infected patient to uninfected patients
by the hands or clothing of staff or other patients [24].
This simple policy for the prevention and management
of postoperative MRSA infections, as well as a greater effort
in screening protocols for MRSA colonization is imperative
in order to allow the reduction of the incidence of noso-
comial MRSA acquisition and invasive infection in cardio-
thoracic patients in the face of continuing endemic risk
[25]. It is important to mention that throughout the 9-year
study period, 826 infectious complications were document-
ed (5.4%) after 15,270 cardiovascular procedures and only
30 reports of MRSA infection (0.2%). Alteration of peri-
operative antimicrobial use in MRSA colonized patients
should be considered, especially in patients undergoing
prosthetic valve or graft implantation. Documentation of
MRSA colonization should be confirmed in the pre-operative
evaluation phase, so that appropriate surveillance for MRSA
infection is performed.

In conclusion, we obtained successful control of MRSA
spread in the OCSC. The prompt determination, isolation
and appropriate treatment of MRSA patients submitted from
other institutions, combined with the detection and elimi-
nation of carriers among new health care workers and
patients at high risk of developing infectious complications,
prevented further spread of the pathogen. If anything has
been learnt about staphylococci in the antimicrobial era,
it is that resistance will follow virtually every class of
drugs. Effective MRSA control remains a major challenge
and has been achieved only by implementing three strin-
gent prophylactic measures before the appearance of MRSA
outbreaks.

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