Significant Reduction of Methicillin-resistant *Staphylococcus aureus* Bacteremia in Geriatric Wards after Introduction of Infection Control Measures against Nosocomial Infections

Hironori Masaki, Hiroshi Watanabe, Satoshi Degawa, Hiroyuki Yoshimine, Norichika Asoh, Naoto Rikitomi, Keizo Matsumoto, Kamruddin Ahmed*, Kiwao Watanabe*, Kazunori Oishi* and Tsuyoshi Nagatake*

**Abstract**

*Objectives*  
(1) To investigate the efficacy of infection control measures against methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremias in geriatric wards.  
(2) To identify predisposing risk factors for MRSA bacteremia.

*Methods*  
Cases with nosocomial bacteremias were retrospectively analyzed between January 1991 and March 1995. The study period was divided into four annual periods and the period 1, January to December 1991, was applied as the control.

*Materials*  
We investigated patients with nosocomial bacteremias in geriatric wards (190 beds) of AINO Memorial Hospital, affiliated with Nagasaki University.

*Results*  
A significant reduction in cases with MRSA-induced nosocomial bacteremia was observed after the introduction of a stringent infection control and prevention program (period 1 vs. periods 2, 3, and 4: p<0.00833, p<0.00167, and p<0.00167, respectively). The major source of bacteremia included urinary tract infections, intravenous catheter-related infections, and infected decubitus ulcers. Improvement of decubitus ulcer was associated with a significant reduction in MRSA bacteremia (period 1 vs. periods 2 and 3: p<0.00017 and p<0.00833).

*Conclusion*  
Stringent infection control programs, including prevention and treatment of decubitus ulcers, are necessary in geriatric wards to reduce and prevent MRSA bacteremia.

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**Key words:** decubitus ulcer, catheter-associated fever, urinary tract infection, respiratory tract infection, povidone iodine

**Introduction**

Nosocomial bacteremia is a major cause of infection in elderly patients where it is often associated with a high mortality rate (1). *Staphylococcus aureus* remains an important cause of nosocomial bacteremias even at present (2–5).

In the United States, strains of methicillin-resistant *Staphylococcus aureus* (MRSA) emerged in the large medical centers in late 1970s (6, 7). In Japan, MRSA became a frequent cause of nosocomial infections in geriatric wards in the early 1980s (8, 9). During the last decade, nosocomial MRSA has also spread across Japan (10). Sakamoto (11) reported several years ago that MRSA infection was endemic and the rate of infection was steadily rising in geriatric wards of a hospital affiliated with Nagasaki University. Based on these findings, strict infection control measures were subsequently initiated to reduce nosocomial infections by MRSA at geriatric wards in our hospital.

In the present study, we analyzed the incidences of nosocomial bacteremias caused by MRSA as well as other bacteria.

**Methods**

**Setting**

AINO Memorial Hospital (AMH), affiliated with Nagasaki University, is a 270-bed acute and long-term care hospital (190 beds, internal medicine including geriatric medicine; and 80 beds, orthopedics) located in the southeast area of Nagasaki prefecture, Japan. It has four 8-bed observation rooms for severely ill patients in geriatric wards. AMH is served by community-based physicians and provides long-term care facilities, because AMH plays an important part not only as a referral center but also as a long-term care hospital. The average hospital stay was approximately 110 days during the 1991–1995 study period. Patients of the geriatric wards (190 beds) were the subjects of the present study, because only a few noso-
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Infection control measures against MRSA

To reduce nosocomial infections, active infection control measures were instituted against MRSA in October 1991, because MRSA infections had increased during the 1980s in spite of strict enforcement of hand cleaning. These measures consisted of the following: 1) Hand washing with disinfectant soap (diethanolamine and propylene glycol, Grince®, Maruishi Seiyaku Co., Osaka) and/or use of disposable non-sterile gloves after hand washing. 2) As a precautionary measures, patients with either colonization or infections with MRSA were isolated. 3) Preventative measures were used to reduce the risk of decubitus ulcer formation by frequent change of body position and disinfection of the ulcer region using 3% of povidone iodine with 70% of sugar (Upasta®), which was applied once a day. 4) To reduce nosocomial infections, active infection control measures were instituted. Disinfection of the upper airway by using 0.03–0.07% of povidone iodine in the oral cavity, which was sprayed into the patient’s mouth twice a day by a Jackson-type nebulizer, and 5% of povidone iodine gel in nasal cavity, which was applied twice a day through the nares, to prevent lower respiratory tract infection (12, 13). 5) Cleaning of the hospital floors using 0.1% benzalkonium chloride was carried out as an environmental disinfectant, applied once daily in geriatric wards and the corridors. Moreover in the observation rooms for severely ill patients such as those in intensive care units (ICUs), the floor disinfectant was used twice a day. The floors were mopped daily prior to the use of benzalkonium chloride. The environmental cleaning was thought to be important, because MRSA was detected not only on the surface of devices such as the tube of the nebulizer, but also as an air-borne bacteria and on the floor in geriatric wards (14). 6) Appropriate antimicrobial chemotherapy for any infection, and 7) education of the staff regarding nosocomial infections.

Aim and study design

The aims of this retrospective study were as follows: 1) to clarify the efficacy of infection control measures against the incidence of MRSA bacteremia, and 2) to identify the predisposing risk factors for MRSA bacteremia. All bloodstream infections were identified by the microbiology laboratory in the hospital, which played an important role in the routine surveillance for MRSA. In this study, we analyzed bloodstream infections caused by pathogenic organisms by dividing the study period into four phases. The period 1 extended from January 1991 to December 1991, period 2 from March 1992 to March 1993, period 3 from April 1993 to March 1994, and period 4 extended from April 1994 to March 1995. Between the period 2 and period 4, the applied infection control measures were similar. During the study period, the clinical judgement of infection control practitioners, hospital epidemiologists, and involved clinicians was maintained at a constant level in spite of the rotation of clinicians, because all physicians practicing at AMH had already received education programs as specialists for infectious diseases and antimicrobial chemotherapy in the department of Internal Medicine, Nagasaki University Hospital. The period 1, although it partly included the early post-intervention period, was considered as a control phase used to analyze the post-intervention effects in each period after introduction of infection control measures. The expanded infection control measures described here were not strictly applied between October and December 1991. Moreover, to determine the post-intervention changes, each period was set up for approximately one year similar to the control period. The incidence and causative organisms of bacteremia were compared with those in each study period.

Clinical information, including the presence of underlying diseases, the source of bacteremia, use of antimicrobial chemotherapy at the onset of bacteremia, use of invasive procedures, presence of bacteremia-associated complications, and the outcome of bacteremia, were obtained from the medical records of participating patients. The outcome of bacteremia cases was categorized as survival, or death within one month after the onset of bacteremia. Nosocomial bacteremia was defined by isolating the organism from blood samples obtained after 48 hours of admission in the hospital. Staphylococcus aureus isolated from blood, or coagulase-negative Staphylococcus (CNS) were considered to be contaminants if the clinicians judged the organisms to be contaminants, and if the antimicrobial chemotherapy directed against the organisms was not administered. Intravascular device-related S. aureus and CNS bacteremia were defined as bacteremia unrelated to infection at an extravascular site. When the catheter was not removed, a culture of a swab taken from tip of the catheter was negative, or the tip was not cultured, the infection was considered to be device-related if the infection control practitioner, or the involved clinicians determined a device to be the likely source.

Blood cultures were immediately performed during high fever (higher than 38°C). However, if sepsis was suspected based on symptoms such as chills and shivering, blood culture was immediately performed in spite of either no or low-grade febrile state. The number of blood cultures in the periods 1 through 4 were as follows: 1,190, 1,116, 700 and 865 specimens. The same technique was used for blood culture during the four periods. During the 1991–1995 study period, the hospital microbiology laboratory used the SEPTI-CHECK (70 ml, Columbia Broth, Becton Dickinson, Heidelberg, Germany) for blood culture if the blood was drawn just before the initiation of antimicrobial chemotherapy; 7 ml of blood sample was inoculated into a culture bottle for aerobic and anaerobic organisms. Whereas during antimicrobial chemotherapy the BACTEC NR 16A (30 ml, Becton Dickinson, Cayey, Puerto Rico, USA) was used for culture of aerobic organisms, and BACTEC NR17A (30 ml, Becton Dickinson, Cayey, Puerto Rico, USA) was used to culture the anaerobic organisms; 7 ml of the blood sample was inoculated into each bottle. Culture of swabs taken from the decubitus ulcer region was routinely performed once every two weeks in patients with such ulcers, to determine whether the ulcer was infected during the post-intervention period. Moreover, cultures of swabs from the decubitus ulcer region were immediately performed when the pa-
tient developed a high fever or when the ulcer was considered to be a focus. The numbers of cultures prepared from decubitus ulcers for the four periods were 494, 366, 420 and 495 specimens, respectively. The method used for culture of swabs from the decubitus ulcer region was the same for all periods. Identification of bacteria was routinely based on culture of various clinical specimens such as sputum, nasal secretion, throat exudate, pus from decubitus ulcer and wound, urine, stool, and blood. API 20E and API 20NE (bioMerieux sa, Lyon, France) were used for identification of gram-positive and -negative bacteria, respectively. For detection of S. aureus, the selection media (salt-mannit media) was additionally used in specimens such as sputum, pus from decubitus ulcer, and stool. The Kirby-Bauer disc sensitivity (Sensi-Disc, Becton Dickinson Microbiology Systems) was used for the \textit{in vitro} antimicrobial susceptibility tests (15). With regard to MRSA, most strains identified as MRSA were resistant to most antibiotics, including methicillin and ceftriaxone as third cephems, except for vancomycin.

\textbf{Statistical analysis}

During the study period, causative organisms of bacteremias and the risk factors of patients with bacteremia were compared by means of the \chi^2 \text{ test} or \text{t}-test. In our analysis, we used the Bonferroni’s method for considering multiple comparisons (16), when appropriate. A \textit{p} value of less than 5% denoted the presence of a statistically significant level. When the \textit{p} value was less than 0.00833, 0.00167, or 0.00017 in the comparison among four periods (six pairs), it was considered to be significant at a level of 5%, 1%, or 0.1%, respectively. When the \textit{p} value was less than 0.0125 or 0.0025 in the comparison of four pairs, it was considered to be significant at a level of 5% and 1%.

\textbf{Results}

\textbf{Patients}

A total of 141 cases out of 193 cases of bacteremia were analyzed in detail. The means (\pm SD), and ranges of age of patients with bacteremia, and the \textit{p} value adjusted for four pairs comparison by Bonferroni’s method were as follows: during the period 1, males 77.0±12.3 (48–90 yr, \textit{n}=32), females 78.8±5.9 (62–93 yr, \textit{n}=109) (mean age, males vs. females: not significant); during the period 2: male’s 74.1±12.5 (49–92 yr, \textit{n}=35), females 80.5±8.5 (55–94 yr, \textit{n}=53), (mean age, males vs. females: \text{p}<0.0125); during the period 3: males 77.9±8.7 (62–86 yr, \textit{n}=7), females 78.5±8.7 (55–94 yr, \textit{n}=47), (mean age, males vs. females: not significant); during the period 4: males 74.7±11.3 (56–90 yr, \textit{n}=20), females 80.6±8.9 (56–92 yr, \textit{n}=37) (mean age, males vs. females: not significant). The mean ages of patients in pre- and post-intervention periods were not statistically different except for those in the period 2.

\textbf{Rate of nosocomial bacteremia}

The rate of bacteremia was significantly diminished during the three-year period under infection control measures as follows: during the periods 1, 2, 3 and 4, 193/501 (38.5%), 88/688 (12.8%), 54/676 (8.0%) and 57/723 (7.9%) discharges, respectively (period 1 vs. periods 2, 3 and 4: \text{p}<0.00017, respectively; period 2 vs. periods 3 and 4: \text{p}<0.00017 and \text{p}<0.00017).

On the other hand, several cases of bacteremia (>2 cases per patient) were observed as follows: period 1, average 3.7 cases in 27 patients; period 2, average 2.7 cases in 21 patients; period 3, average 2.5 cases in 12 patients; period 4, average 3.1 cases in 9 patients. The frequencies of \textit{S. aureus} bacteremia, considered as a contamination, during the periods 1, 2, 3 and 4 were period 1, methicillin-sensitive \textit{S. aureus} (MSSA) 0 and MRSA 0 case; period 2, MSSA 3 and MRSA 0 case; period 3, MSSA 2 and MRSA 2 cases; and period 4, MSSA 1 and MRSA 2 cases, respectively.

\textbf{Underlying diseases}

The underlying diseases associated with bacteremia are shown in Table 1. The most common underlying disease in AMH was cerebrovascular diseases which accounted for 47.7–73.0%. The next common underlying disease was decubitus ulcer, which was associated with the long-term bed ridden condition, such as cerebrovascular diseases or fracture of the femur. After infection control measures the rate of MRSA isolated in the decubitus ulcer diminished to <20%. Moreover, the rate of MRSA isolated from patients with large and severe decubitus ulcer of Stage IV (17) was also diminished (18).

\textbf{Causative organisms of bacteremia}

Causative organisms of bacteremia during the study periods are shown in Fig. 1. After control measures were instituted, the rate of MRSA bacteremia diminished significantly during the study periods as follows: during the periods 1, 2, 3 and 4, 64/193 (33.2%), 14/88 (15.9%), 5/54 (9.3%), and 5/57 (8.8%), respectively (period 1 vs. periods 2, 3 and 4: \text{p}<0.00833, \text{p}<0.00167, \text{p}<0.00017, respectively). In gram-positive cocci, the prevalence of MSSA and CNS did not change significantly, with the exception of MRSA. In gram-negative rods, the percentage of cases infected with \textit{Escherichia coli} and \textit{Proteus mirabilis} significantly increased (\textit{E. coli}, period 1 vs. periods 2 and 4: \text{p}<0.00833 and \text{p}<0.00017; and \textit{P. mirabilis}, period 1 vs. period 3: \text{p}<0.00167). For anaerobic bacteria, there was no significant reduction of \textit{Bacteroides fragilis}. In urinary-tract infections, MRSA bacteremia was found in 1, 0, 0 and 1 cases during the four periods, respectively. In central venous catheter-associated infections, MRSA bacteremia was detected in 6, 3, 0 and 1 cases during periods 1, 2, 3 and 4, respectively.

\textbf{Sources of bacteria (Table 2)}

Sources of bacteria are shown in Table 2. In the period 1, the most common source was infected decubitus ulcer, which accounted for approximately 50%. The next common sources were the urinary tract (17%) and the central venous catheter (15.6%). After infection control measures, the frequency of decubitus ulcer as a source of bacteremia diminished to 18.3–29.5% compared with that of the period 1. (period 1 vs. peri-
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Table 1. Underlying Diseases Diagnosed in the Study Population in Each of the Four Periods

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (n=141)</th>
<th>Period 2 (n=88)</th>
<th>Period 3 (n=54)</th>
<th>Period 4 (n=57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrovascular disease</td>
<td>103 (73.0%)</td>
<td>42 (47.7%)</td>
<td>39 (72.2%)</td>
<td>39 (68.4%)</td>
</tr>
<tr>
<td>Decubitus ulcer with MRSA colonization</td>
<td>101 (71.6%)</td>
<td>44 (50.0%)</td>
<td>25 (46.3%)</td>
<td>32 (56.1%)</td>
</tr>
<tr>
<td>Bone fracture</td>
<td>26 (18.4%)</td>
<td>3 (3.4%)</td>
<td>10 (18.5%)</td>
<td>14 (24.6%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (6.4%)</td>
<td>15 (17.0%)</td>
<td>8 (14.8%)</td>
<td>17 (29.8%)</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>15 (10.6%)</td>
<td>9 (10.2%)</td>
<td>14 (25.9%)</td>
<td>7 (12.3%)</td>
</tr>
<tr>
<td>Chronic heart failure</td>
<td>13 (9.2%)</td>
<td>5 (5.7%)</td>
<td>10 (18.5%)</td>
<td>10 (17.5%)</td>
</tr>
<tr>
<td>Malignant tumor</td>
<td>11 (7.8%)</td>
<td>14 (15.9%)</td>
<td>5 (9.3%)</td>
<td>11 (19.3%)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>1 (0.7%)</td>
<td>10 (11.4%)</td>
<td>4 (7.4%)</td>
<td>6 (10.5%)</td>
</tr>
<tr>
<td>Ileus</td>
<td>13 (9.2%)</td>
<td>19 (21.5%)</td>
<td>4 (7.4%)</td>
<td>4 (7.0%)</td>
</tr>
</tbody>
</table>

ods 2 and 3: p<0.00017 and p<0.0083; period 2 vs. period 4: p<0.0083). In the same way, after infection control measures, the frequency of MRSA isolated from the decubitus ulcer also reduced to 16.1–22.5% (period 1 vs. period 2: p<0.00167). On the other hand, the percentage of cases with urinary-tract infection significantly increased during the study (period 1 vs. periods 3 and 4: p<0.00833 and p<0.00833). Urinary-tract infection remained a major source of bacteremia during the study periods.

Invasive medical procedures

At the onset of bacteremia, the major invasive medical procedures were insertion of indwelling urinary catheters and central venous catheters. The indwelling urinary catheter was associated with 89, 63, 39 and 34 cases of nosocomial infections during the four periods, respectively. The central venous catheter was associated with 76, 63, 33, and 26 cases of nosocomial infections during the periods 1, 2, 3 and 4, respectively. Combination of urinary catheter and central venous catheter-related bacteremias was found in 68, 52, 33 and 26 cases during the periods 1, 2, 3 and 4, respectively. The number of cases with bacteremia associated with medical procedures such as an indwelling urinary catheter, central venous catheter, and nasogastric tube diminished with the control of nosocomial infections (central venous catheter: period 1 vs. period 2, p<0.0083; nasogastric tube: period 1 vs. periods 2, 3 and 4: p<0.00167, p<0.00167, and p<0.00833). However medical procedures described above were performed in 70–90% of bacteremic cases during the study period.

Complications and prognosis of bacteremia

The major complications in patients with bacteremia were disseminated intravascular coagulation (DIC) and septic shock. DIC was noted in 17, 24, 5 and 7 cases during the periods 1, 2, 3 and 4, respectively. Furthermore, septic shock was observed in 18, 17, 10 and 7 cases during the periods 1, 2, 3 and 4, respectively. The number of cases with DIC and septic shock diminished with reductions in the rate of nosocomial infec-
Figure 1. Causative organisms of bacteremia in each of the four periods. *: Significance of rate of MRSA bacteremia, #: Significance of rate of nosocomial bacteremia. Statistically significant level: p<0.00833, 5% (*, #) p<0.00167, 1% (**, ##) ; p<0.00017, 0.1% (***, ###).

Discussion

The emergence of MRSA was first described in 1961 (19). In large medical centers in the United States about twenty years ago, epidemic outbreaks caused by MRSA were recognized (6, 7). MRSA is of special concern particularly in nursing homes because these institutions might serve as reservoirs for MRSA in the community (20). A high incidence of MRSA infection or colonization was identified in nursing home patients (21). Furthermore, decubitus ulcers are common problems in nursing homes and are associated with significant morbidity and mortality (17).

In Japan during the early 1980s, MRSA emerged as a frequent cause of nosocomial infections in the geriatric ward (6, 7), which, to some extent, could be considered as a nursing home. Our results demonstrated the presence of extremely high rates of nosocomial bacteremia during the study periods. We believe the reason for these findings include long-term bed rest, high percentage of elderly patients, patients with recurrent bacteremias, and severe infection of decubitus ulcers in our geriatric wards. These conditions are different from those of community hospitals (22). In infection control measures, hand washing is one of the most important measures against MRSA, because the principal mode of transmission is via the transiently colonized hands of hospital personnel (23). However, in geriatric wards of AMH, hand washing was not the only contributer to the reduction in MRSA infection cases. Just before the introduction of infection control measures, the risk factors for MRSA infections in patients were defined in the geriatric wards of AMH (12). Colonization of MRSA in the upper airway and decubitus ulcers was significantly higher in seriously ill patients than in moderately ill patients. Moreover, a high frequency of infections and antimicrobial chemotherapy was observed in such patients. Therefore, the infection control measures were based on the fact that colonization of MRSA was seen frequently in the upper airway and decubitus ulcers. The other infection control measures to be emphasized were prompt isolation, disinfection of the upper airway, disinfection of the decubitus ulcer, and daily cleaning of the floors (11).

In fact, after the introduction of infection control measures,
we observed a fall in the percentage of patients with severely infected decubitus ulcers, which was the most common source of bacteremia. During the study period, however, the total number of decubitus ulcers in the geriatric ward did not diminish in spite of the preventative control measures because new patients with decubitus ulcers were continuously admitted to our hospital after being referred from other hospitals. The number of invasive medical procedures was also significantly reduced. Moreover, the number of cases of bacteremia, particularly MRSA bacteremia, was also significantly reduced. This successful infection control program for decubitus ulcers mainly explained the significant reduction of bacteremia. We believe that the reduction in the rate of MRSA colonization and the decrease in recurrent bacteremias were probably due to the low rate of severely infected decubitus ulcers. On the other hand, disinfection of the upper airway, which resulted in the elimination of S. aureus colonized in nasal and oral passages, has been considered to be important in the reduction of cases with lower respiratory tract infections (12, 13). Several additional problems such as old age, presence of underlying diseases, decline of mental activity, presence of decubitus ulcers, difficulties with oral feeding, and a decline in overall systemic immunity also existed in patients with long-term bed-ridden conditions admitted to the geriatric wards of AMH (22). Previous studies have shown that the risk factors for bacteremia included a longer mean hospital stay, treatment with antibiotics before infections, length of prior hospitalization, and invasive procedures (24, 25). With regard to appropriate antimicrobial chemotherapy of infections during the post-intervention periods, the total dose of antimicrobial agents used in our patients was reduced, together with reduced use of second and third cephems, while the use of penicillins was increased. However, the susceptibility of S. aureus to such changes in antibiotic use has not yet improved except for a partial restoration of sensitivity to minocycline (26).

In conclusion, the results of the present study indicate that for a proper and clinically meaningful reduction of nosocomial bacteremia such as MRSA bacteremia in geriatric wards, extensive infection control measures, in addition to hand washing, should be designed for the infection control of decubitus ulcers and prevention of decubitus ulceration.
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