MAJOR ARTICLE

Salvage Treatment for Persistent Methicillin-Resistant *Staphylococcus aureus* Bacteremia: Efficacy of Linezolid With or Without Carbapenem

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Background. Persistent methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia is associated with high mortality rates, but no treatment strategy has yet been established. We performed this study to evaluate the efficacy of linezolid with or without carbapenem in salvage treatment for persistent MRSA bacteremia.

Methods. All adult patients with persistent MRSA bacteremia for ⩾7 days from January 2006 through March 2008 who were treated at Seoul National University Hospital were studied. The results of linezolid salvage therapy with or without carbapenem were compared with those of salvage therapy with vancomycin plus aminoglycosides or rifampicin.

Results. Thirty-five patients with persistent MRSA bacteremia were studied. The early microbiological response (ie, negative results for follow-up blood culture within 72 hours) was significantly higher in the linezolid-based salvage therapy group than the comparison group (75% vs 17%; $P = .006$). Adding aminoglycosides or rifampicin to vancomycin was not successful in treating any of the patients, whereas linezolid-based therapy gave an 88% salvage success rate ($P < .001$). The *S. aureus*–related mortality rate was lower for patients treated with a linezolid salvage regimen than for patients continually treated with a vancomycin-based regimen (13% vs 53%; $P = .030$).

Conclusions. Linezolid-based salvage therapy effectively eradicated *S. aureus* from the blood for patients with persistent MRSA bacteremia. The salvage success rate was higher for linezolid therapy than for vancomycin-based combination therapy.

Staphylococcus aureus is a major cause of community-acquired and nosocomial infections [1]. The organism is the second most common cause of nosocomial bacteremia in the United States [2]. Glycopeptides have been used as the main treatment for serious methicillin-resistant *S. aureus* (MRSA) infections, including bacteremia. However, treatment failure in MRSA infections has increased and has become a major clinical problem [3–5].

Persistent *S. aureus* bacteremia raises concern because it occurs despite the administration of appropriate antibiotics shown by laboratory tests to be active in vitro. The microbiological and clinical characteristics of persistent *S. aureus* bacteremia have been studied [6–9], but the mechanism of persistence is still poorly understood, and no clinical indicator is available to predict glycopeptide treatment failure. Moreover, no treatment strategy has been established, despite the fact that failure is common and frequently leads to death [8, 9]. The approaches of infectious diseases consultants to treating persistent MRSA bacteremia have been examined [10], but no consensus has emerged in relation to antimicrobial therapy because few clinical data are available.

Linezolid, an oxazolidinone, is used to treat infections caused by resistant gram-positive pathogens. Its efficacy in treating skin and soft-tissue infections, pneu-

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monia, and uncomplicated MRSA bacteremia is not inferior to that of vancomycin [11]. However, its efficacy in treating endocarditis or complicated or persistent bacteremia has not been clearly defined. Recent studies have shown that the combined use of linezolid and carbapenem has a synergistic bactericidal effect on *S. aureus* in vitro and in an animal endocarditis model [12, 13], but no clinical data are available. We performed this study to investigate the incidence and clinical features of persistent *S. aureus* bacteremia and to estimate the efficacy of linezolid with or without carbapenem for the salvage treatment of persistent *S. aureus* bacteremia.

PATIENTS AND METHODS

Patients. All patients ⩾16 years old with persistent *S. aureus* bacteremia from 1 January 2006 through 31 March 2008 were studied at Seoul National University Hospital (Republic of Korea), a 1500-bed tertiary care university hospital and referral center. Patients were identified by reviewing the computerized records of the Clinical Microbiology Laboratory. Only the first episode of *S. aureus* bacteremia in a patient was included in the study.

Microbiological tests. *S. aureus* was identified and antibiotic resistance was determined with automated systems (Vitek 2, bioMérieux; and Microscan, Dade Behring). Susceptibility to arbekacin was determined by the disk diffusion method with 30-μg arbekacin disks (Eiken Chemical) and a breakpoint of ⩾18 mm. In cases of MRSA, the minimum inhibitory concentration (MIC) of vancomycin was determined by microdilution (BBL Mueller Hinton II Broth [cation adjusted]; BD Diagnostics) in accordance with the recommendations of the Clinical and Laboratory Standards Institute [14]. Screening tests for hetero-vancomycin-intermediate *S. aureus* (hetero-VISA) were performed using brain heart infusion agar plates containing 4 μg/mL of vancomycin [15].

Definitions. Persistent bacteremia was defined as the isolation of *S. aureus* in blood cultures obtained from peripheral veins on ⩾7 consecutive days despite appropriate antibiotic administration for ⩾5 days. *S. aureus* bacteremia was defined as community associated or as health care associated in accordance with Centers for Disease Control and Prevention definitions [16]. *S. aureus* infection was defined as catheter related if the catheter tip yielded >15 colonies for *S. aureus* or inflammation was present at the insertion site and no alternative source of infection was identified [17]. Endocarditis was defined by the modified Duke criteria [18]. Metastatic infection was defined as the presence of microbiological or radiographic evidence of *S. aureus* infection caused by hematogenous seeding [19]. Complicated infection was defined as a site of infection remote from the primary focus caused by hematogenous seeding, including endocarditis, or extension of the infection beyond the primary focus (eg, septic thrombophlebitis or abscess) [20]. Eradicable foci included surgically removable infections or drainable abscesses and indwelling foreign bodies, such as peripheral and central venous catheters. Noneradicable foci included unknown primary sites, pneumonia, endocarditis, and osteomyelitis or arthritis. Noneradicated foci comprised noneradicable foci and eradicable foci not actually eradicated [21]. Thirty-day mortality was defined as the death of a patient without clearance of bacteremia or within 30 days after clearance of bacteremia. Mortality was defined as *S. aureus*–related if there was no other definite cause of death.

Salvage attempt and outcome measure. Salvage attempt was defined as administration of a new antibiotic, active against the *S. aureus* isolate in laboratory susceptibility tests, for ⩾72 hours as a substitute or supplement. Linezolid was administered intravenously at a dosage of 600 mg every 12 hours as salvage therapy. The efficacy of salvage treatment was evaluated by 2 outcome measures: early microbiological response and salvage success. Early microbiological response was defined as conversion of positive blood culture results to negative within 72 hours of antibiotic initiation. Salvage was defined as successful if the agent used was not subsequently changed because of ineffectiveness and *S. aureus*–related death did not occur.

Statistical analysis. Categorical variables were compared using the Fisher exact test or Pearson χ^2 test, as appropriate, and continuous variables were compared using the Mann-Whitney *U* test. All tests of significance were 2-tailed, and $P \leqslant .05$ was considered statistically significant. Statistical analyses were performed with SPSS, version 12.0 (SPSS).

RESULTS

Prevalence of persistent S. aureus bacteremia. We identified 377 cases of *S. aureus* bacteremia during the study period. Of the 377 cases of *S. aureus* bacteremia, 41 (11%) were persistent despite administration of appropriate antibiotic. Thirty-five (17%) of the 211 cases of MRSA bacteremia and 6 (4%) of the 166 cases of methicillin-sensitive *S. aureus* (MSSA) bacteremia were persistent ($P < .001$). The duration of persistence was 7–10 days (median, 7 days; mean, 7.6 days) for the cases of MSSA bacteremia and 7–168 days (median, 12 days; mean, 18.1 days) for the cases of MRSA bacteremia ($P = .009$). All the patients with persistent MSSA bacteremia were successfully treated using nafcillin-penicillin with or without aminoglycoside (plus rifampicin in the case of prosthetic valve endocarditis), so salvage attempt was not applied for them.

Clinical characteristics of persistent MRSA bacteremia. Of the 35 cases of MRSA bacteremia, 34 were health care associated (30 nosocomial) and 1 was community associated. The clinical features of the persistent cases of MRSA bacteremia are given in tables 1 and 2. The mean age of the patients was 59 years in the vancomycin-continued group and 70 years in the linezolid salvage group ($P = .01$). For the 35 patients, diabetes

Table 1. Clinical Features and Outcomes of Persistent Methicillin-Resistant *Staphylococcus aureus* Bacteremia in 19 Patients Treated with Vancomycin-Based Regimens

Patient identifier	Duration of bacteremia, days	Vancomycin MIC, μg/mL	Serum vancomycin trough level reached, μg/mL	Result of screening for hetero-VISA	Final regimen	Underlying disorder	Primary site	Complicated or metastatic infection	Adjunctive therapy	Complete removal of infection foci by adjunctive therapy	Outcome
1	7	1.0	7.5	–	Vancomycin	DM, ESRD	Central catheter	Vascular graft infection, brain abscess, septic lung	Catheter removal	–	Died
2	8	1.0	11.9	–	Vancomycin	Stomach cancer, hemodialysis	Central catheter	–	Catheter removal	+	Died
3	8	1.0	16.0	+	Vancomycin	DM, stroke, CABG	Operation site	Mediastinitis	I & D, mediastinum	–	Cured
4	8	2.0	10.2	+	Vancomycin	ESRD	Central catheter	Vascular graft infection, spondylitis, septic lung	Catheter removal	–	Cured
5	10	1.0	16.5	–	Vancomycin	DM, paraplegia	Sore	Spondylitis, empyema	Thoracostomy I & D, sore	–	Cured
6	11	1.0	11.1	–	Vancomycin	Esophageal cancer	Operation site	Mediastinitis	–	–	Cured
7	11	1.0	6.3	–	Vancomycin	Sudden cardiac arrest	Central catheter	Venous thrombus	Catheter removal	–	Cured
8	11	1.0	22.2	–	Vancomycin	DM, ESRD	Pneumonia	–	–	–	Died
9	11	1.0	10.4	+	Vancomycin	Acute myeloid leukemia	Central catheter	Venous thrombus, brain abscess	Catheter removal	–	Died
10	11	1.0	11.2	–	Vancomycin	Rectal cancer	Operation site	Perianal abscess	–	–	Died
11	14	1.0	18.1	–	Vancomycin	DM, ESRD	Central catheter	Venous thrombus, endocarditis	Catheter removal, thrombectomy valve replacement	+	Cured
12	14	1.0	12.7	–	Vancomycin	DM, ESRD, liver cirrhosis	Central catheter	Mycotic aneurysm	Catheter removal	–	Cured
13	18	1.0	23.0	–	Vancomycin	Stomach cancer, hepatocellular carcinoma	Central catheter	–	Catheter removal	+	Died
14	22	1.0	38.4	–	Vancomycin	Stroke	Endocarditis	Brain emboli	Valve replacement	–	Cured
15	10	1.0	6.1	–	Vancomycin and gentamicin	–	Endocarditis	Brain emboli, meningitis	–	–	Cured
16	9	1.0	13.6	–	Vancomycin and arbekacin	DM, lymphoma	Pneumonia	–	–	–	Died
17	10	1.0	30.8	–	Vancomycin, arbekacin, and rifampicin	Prosthetic valve	Central catheter	Endocarditis, brain emboli	Catheter removal, valve replacement	–	Died
18	14	1.0	26.7	+	Vancomycin and rifampicin	Colon cancer, hemodialysis	Central catheter	Endophthalmitis	Catheter removal	–	Died
19	17	0.5	12.7	–	Vancomycin and rifampicin	Prosthetic valve	Central catheter	Brain emboli	Catheter removal	–	Died

NOTE. CABG, coronary artery bypass graft; DM, diabetes mellitus; ESRD, end-stage renal disease; I & D, incision and drainage; MIC, minimum inhibitory concentration; VISA, vancomycin-intermediate *S. aureus*. Plus sign indicates positive; minus sign, negative.

Table 2. Clinical Features and the Consequences of Linezolid-Based Salvage Therapy in 16 Patients with Persistent Methicillin-Resistant *Staphylococcus aureus* Bacteremia

Patient identifier	Duration of bacteremia, days	Vancomycin MIC, μg/mL	Serum vancomycin trough level reached, μg/mL	Final regimen	Underlying disorder	Primary site	Complicated or metastatic infection	Adjunctive therapy	Complete removal of infection foci by adjunctive therapy	Salvage success	Outcome
1	13	1.0	12.9	Linezolid	DM, ESRD	Vascular graft	Spondylitis, epidural abscess	Graft removal	–	Yes	Cured
2	168	1.0	18.3	Linezolid	Aortic dissection, graft	Vascular graft	Empyema, mediastinitis	I & D, mediastinum, empyema	–	Yes	Cured
3	25	2.0	14.7	Linezolid	DM, ESRD, prosthetic valve	Endocarditis	Endocarditis	Valve replacement	+	Yes	Died (of *Enterobacter* bacteremia)
4	13	1.0	24.1	Linezolid	Hepatocellular carcinoma	Liver abscess	Spondylitis, epidural abscess	Abscess percutaneous drainage	–	Yes	Cured
5	14	1.0	24.4	Linezolid and imipenem	DM, ESRD	Central catheter	Graft thrombus, septic lung	Catheter removal, graft removal	–	Yes	Cured
6	41	1.0	20.8	Linezolid and ertapenem	ESRD	Vascular graft	Spondylitis	Graft removal	–	Yes	Cured
7	18	1.0	16.1	Linezolid and ertapenem	DM, multiple myeloma	DM foot	Epidural and psoas abscess, endophthalmitis, septic lung	–	–	Yes	Cured
8	8	1.0	–	Linezolid	Aortofemoral graft	Pneumonia	Spondylitis, epidural abscess	–	–	Yes	Cured
9	31	1.0	15.2	Linezolid and ertapenem	CABG, bladder cancer	Pneumonia	Spondylitis, epidural abscess, brain emboli	–	–	Yes	Cured
10	7	1.0	15.5	Linezolid and ertapenem	Lung cancer	Central catheter	Venous thrombus	Catheter removal	–	Yes	Cured
11	12	1.0	21.7	Linezolid and ertapenem	DM, esophageal cancer	Operation wound	Deep neck abscess	Abscess percutaneous drainage	–	Yes	Cured
12	19	2.0	27.3	Linezolid and meropenem	Aortoiliac graft	Pneumonia	–	–		Yes	Cured
13	8	1.0	14.1	Linezolid	Acute myeloid leukemia	Central catheter	–	Catheter removal	+	Yes	Cured
14	11	1.0	18.0	Linezolid	Waldenstrom's macroglobulinemia	Pneumonia	–	–	–	Yes	Died (of *Klebsiella* bacteremia)
15	14	0.5	18.0	Linezolid and meropenem	ESRD	Central catheter	Venous thrombus, septic lung	Catheter removal	–	No	Died
16	21	1.0	26.7	Linezolid and ertapenem	Spine prosthesis	Spondylitis	Epidural abscess	Epidural abscess removal	–	No	Died

NOTE. CABG, coronary artery bypass graft; DM, diabetes mellitus; ESRD, end-stage renal disease; I & D, incision and drainage; MIC, minimum inhibitory concentration. Plus sign indicates positive; minus sign, negative.

Table 3. Results of 28 Salvage Attempts for 35 Patients with Persistent Methicillin-Resistant *Staphylococcus aureus* Bacteremia

Salvage method	No. of attempts	Early microbiological response,[a] no. (%) of patients	Salvage success,[b] no. (%) of patients
Addition of aminoglycosides[c] or rifampicin[d] to vancomycin	12	2 (17)	0 (0)
Vancomycin and aminoglycosides	6	0 (0)	0 (0)
Vancomycin and rifampicin	4	1 (25)	0 (0)
Vancomycin, aminoglycosides, and rifampicin	2	1 (50)	0 (0)
Substitution of linezolid for vancomycin	16	12 (75)	14 (88)
Linezolid	7	5 (71)	7 (100)
Linezolid and carbapenem	9	7 (78)	7 (78)

[a] Negative results for follow-up blood culture within 72 h after administration of salvage antibiotic ($P = .006$, derived by comparing addition of aminoglycosides or rifampicin to vancomycin with substitution of linezolid for vancomycin).
[b] $P < .001$ (derived by comparing addition of aminoglycosides or rifampicin to vancomycin with substitution of linezolid for vancomycin).
[c] Gentamicin was used in 2 cases in which the isolates were susceptible to gentamicin, whereas arbekacin was used in the other cases in which the isolates were resistant to gentamicin but susceptible to arbekacin.
[d] Rifampicin was used in 6 cases in which the isolates were susceptible to rifampicin.

mellitus (in 12 patients [34%]), end-stage renal disease (in 10 [29%]), solid cancers (in 10 [29%]), and the presence of vascular grafts (in 11 [31%]) were common as underlying disease. Endovascular infection (in 19 patients [54%]), especially of a central catheter (in 15 [43%]), was the most common primary site of infection. Twenty-eight (80%) of the cases were complicated *S. aureus* infections. Infected venous thrombus and abscess were detected in 7 (20%) and 14 (40%) of the cases, respectively. Transthoracic echocardiography and transesophageal echocardiography were performed in 30 (86%) and 13 (37%) of the patients with MRSA bacteremia, respectively. Endocarditis was detected in 6 patients (17%). Metastatic foci were observed in 20 patients (57%), and common metastatic foci were endovascular structures (endocardium or vascular grafts) (in 9 patients), spine (in 8), brain (in 7), lung (in 5), and pleura (in 2). Although adjunct therapy to remove foci was performed in 25 patients (71%), noneradicated foci remained in 30 patients (86%). Underlying diseases, primary site of infection, rates of complicated and metastatic infection, and noneradicated foci were not significantly different in the vancomycin-continued and linezolid salvage groups.

Among the 35 MRSA isolates causing persistent bacteremia, the vancomycin MIC was 2 μg/mL in 3 isolates. No VISA was observed. Four isolates (11%) showed growth on brain heart infusion agar with 4 μg/mL of vancomycin. Resistance to gentamicin and rifampicin was observed in 25 (71%) and 3 (9%) of the cases, respectively. All the isolates were susceptible to linezolid and arbekacin. MRSA bacteremia was persistent, although the serum vancomycin trough concentration exceeded 10 μg/mL in 31 (91%) and 15 μg/mL in 19 (56%) of the 34 cases evaluated in our study.

Salvage antibiotic attempts and outcomes for patients with persistent MRSA bacteremia. The salvage attempts against persistent MRSA bacteremia and their consequences are summarized in tables 3 and 4. Early microbiological responses and salvage success rates were significantly higher with the linezolid-based regimen than with the comparators ($P = .006$ and $P < .001$, respectively). Adding aminoglycosides or rifampicin to

Table 4. Mortality Rates in 35 Patients with Persistent Methicillin-Resistant *Staphylococcus aureus* Bacteremia

Patient group	No. of patients	*S. aureus*–related mortality,[a] no. (%) of patients	30-day mortality,[b] no. (%) of patients
Vancomycin-continue group	19	10 (53)	10 (53)
Vancomycin	14	6 (43)	6 (43)
Vancomycin and aminoglycosides or rifampicin	5	4 (80)	4 (80)
Linezolid salvage group	16	2 (13)	4 (25)
Linezolid	7	0 (0)	2 (29)
Linezolid and carbapenem	9	2 (22)	2 (22)

[a] $P = .030$ (derived by comparison of the vancomycin-continue group and linezolid salvage group).
[b] $P = .166$ (derived by comparison of the vancomycin-continue group and linezolid salvage group).

vancomycin was not successful in any case. However, linezolid-based therapy had a salvage success rate of 88%. A linezolid-based regimen was introduced for 6 patients who had treatment failure despite the addition of aminoglycosides or rifampicin. One of these patients died without a microbiological response, but 4 of the others became culture negative within 72 hours and the remaining patient within a week. These 5 patients were successfully treated.

The 30-day mortality rate was 40% (14 patients) and the *S. aureus*–related mortality rate was 34% (12 patients) for the 35 patients with persistent MRSA bacteremia. The *S. aureus*–related mortality rate was significantly lower for patients who were treated with a linezolid salvage regimen than for patients who were continuously treated with a vancomycin-based regimen (53% vs 13%; $P = .03$; table 4).

Adverse reactions to linezolid-based therapy. Seven (58%) of 12 evaluable patients had linezolid-associated thrombocytopenia during use of the antibiotic. Thrombocytopenia developed 7–21 days after the initiation of antibiotic treatment. Linezolid-based regimens were changed to vancomycin with or without rifampicin in 7 patients. Of these, 5 were successfully treated. However, recurrence of bacteremia was observed in 2 patients, and they were successfully treated by readministration of linezolid with or without carbapenem.

DISCUSSION

In the present study, we found that linezolid-based salvage therapy was effective in eradicating *S. aureus* from the blood within 72 hours for patients with persistent MRSA bacteremia. We also showed that the salvage success rate was higher with linezolid-based therapy than with vancomycin-based combination therapy. The rate of persistence of *S. aureus* bacteremia was 11% during the study period in our hospital. This figure had not increased: it was 13% (31 of 238 patients with *S. aureus* bacteremia) in our previous investigation from January 1998 to October 2001 [22]. The prevalence in our hospital was similar to that in another center, with 11% of persistent bacteremia for ⩾7 days [9]. Persistence was more common in MRSA bacteremia than in MSSA bacteremia, which agrees with previous studies [8, 9].

Some investigators have reported cases of persistent bacteremia caused by VISA or hetero-VISA [23, 24]. However, we found no VISA, and only 4 isolates were positive on the hetero-VISA screening test. In addition, only a few isolates had a vancomycin MIC of 2 μg/mL. Similar findings were obtained in other studies [7, 8]. Adequate vancomycin serum concentration is important to eradicate MRSA from infected sites. However, MRSA bacteremia persisted even though serum vancomycin trough concentrations exceeded 10 μg/mL in most of the patients evaluated in our study. Some authors have proposed that it is important to achieve serum vancomycin trough concentrations of >15 μg/mL to achieve better treatment outcomes in MRSA infections [25]. However, 56% of our patients had persistent bacteremia despite the fact that their serum vancomycin trough concentrations were >15 μg/mL.

Approximately 70% of infectious diseases consultants in the United States reported that they preferred to continue administration of vancomycin and add aminoglycoside or rifampicin for persistent MRSA bacteremia if the vancomycin MIC did not exceed 2 μg/mL [10]. We also used these agents in addition to vancomycin for patients with persistent MRSA bacteremia that did not response to vancomycin monotherapy. Of the aminoglycosides, gentamicin was used for 2 patients, whereas arbekacin was used for the patients for whom the isolates were resistant to gentamicin but susceptible to arbekacin [26]. However, these attempts were unsuccessful: combination therapy was ineffective for most of the patients for whom vancomycin alone had failed to eradicate *S. aureus* from the blood.

The success rate of salvage attempts with linezolid-based regimens was 88% in the present study, and similar success rates have been reported in previous studies [24, 27]. Although the number of cases was small, linezolid seemed to be effective as salvage therapy in our study, even though the regimen was introduced for patients for whom vancomycin-based combination therapy had already failed or who had had persistent MRSA bacteremia for a prolonged period or who had multiple metastatic sites. We chose ertapenem for combination therapy in our study because it has the narrowest spectrum among carbapenems.

Various new antibiotics could be considered candidates for the treatment of persistent MRSA bacteremia [28]. However, good penetration of the antibiotic into the tissues of the body, especially lung, bone, and brain, and if possible into biofilms, abscesses, thrombi, and cardiac vegetations is essential, because devices, abscesses, thrombi, endocarditis, and metastatic foci at various sites were shown in our study and in others [8, 9] to be implicated in bacteremic persistence. We tried linezolid and carbapenem, which synergize, because both have good tissue-penetration properties.

Although the efficacy of linezolid-based regimens was good, thrombocytopenia limited their prolonged use for the ⩾4 weeks that are needed to treat complicated *S. aureus* bacteremia [1]. The incidence of thrombocytopenia in our study was high, probably because of the high proportion of serious underlying diseases and end-stage renal disease for patients with persistent bacteremia [29]. Although the duration of linezolid therapy was shortened by thrombocytopenia, the subsequent use of vancomycin for a total of 4–6 weeks after negative blood culture results were achieved was successful.

The present study has methodological limitations because it was retrospective in design. Hence, regimen, starting point, and duration of salvage therapy were not uniform. Because the

factors influencing the physicians' choice of antibiotics were not determined, they may have influenced our results as unmeasured confounding factors in the analysis. Also, the sample size was limited and too small to distinguish between the effectiveness of linezolid-carbapenem combination therapy and linezolid monotherapy. The prevalence of endocarditis was possibly underestimated because transesophageal echocardiography was performed in only 37% of the patients. Despite such limitations, our data provide some valuable information that can affect treatment strategy. No clinical data were previously available on the outcome of salvage therapy that compared the use of alternative agents with the addition of aminoglycosides or rifampicin to vancomycin for patients with persistent MRSA bacteremia. Moreover, the clinical outcome of combination treatment with linezolid and carbapenem for patients with persistent MRSA bacteremia was defined for the first time.

In summary, for treating persistent MRSA bacteremia, the substitution of alternative agents for vancomycin appeared to be preferable to the addition of rifampicin or aminoglycoside to vancomycin, even if the isolate involved has been reported by current laboratory tests to be susceptible to vancomycin. Linezolid with or without carbapenem can be an effective salvage option, producing better outcomes for patients with persistent MRSA bacteremia.

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