An Antibiotic Care Bundle Approach Based on Results of Rapid Molecular Screening for Nasal Carriage of Methicillin-resistant *Staphylococcus aureus* in the Intensive Care Unit

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**Abstract.** The potential role of active methicillin-resistant *Staphylococcus aureus* (MRSA) surveillance in the intensive care unit (ICU), has been recently proposed as a guide for antibiotic treatment in patients suspected of being infected with MRSA by using an antibiotic care bundle (ACB) approach. A group of 376 consecutive ICU patients were prospectively screened for nasal carriage of MRSA using a real-time polymerase chain reaction test. The study group consisted of 244 (64.9%) males and (35.1%) females, with a median age of 64 (range 17-95 years). Overall, 26 (6.9%) patients were positive for MRSA, while 350 (93.1%) were MRSA-negative. No difference was observed in gender and age between groups. During ICU stay, 9 (2.4%) patients developed generalized MRSA infection, of whom 8 out of 26 (30.8%) were MRSA-carriers and one out of the 350 (0.3%) was MRSA-negative. Thus, a strong relationship between MRSA infection and MRSA carriage (relative risk=107.7, 95% confidence interval=14.0-828.5, p<0.0001) was found. Subsequently, in our ICU, we developed and introduced a new ACB approach based on rapid nasal screening results for improving the management of critically ill patients. The use of anti-MRSA agents should be re-evaluated daily on the basis of clinical and laboratory features, with positive cultures from sterile site or signs of active infection supporting prolongation of empirical treatment. On the contrary, MRSA-negative clinical cultures support a de-escalation strategy. In conclusion, the early identification of MRSA-carriers using a rapid molecular screening is safe and accurate, allowing MRSA-positive patients, who will more likely develop MRSA infections, to be detected.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of community-acquired infections in hospitalized patients, especially on those admitted to critical areas, such as intensive care units (ICU) (1-3). MRSA has a tendency to affect the skin and the soft tissues, but invasive infections including pneumonia, bacteremia and endocarditis have been reported as well (4). Thus, patients, MRSA-carriers, should be monitored closely, being at higher risk as compared with MRSA-free patients (5, 6). Earlier identification of nasal carriers of MRSA is considered essential, both to prevent and limit the spread of resistant strains, and to reduce the MRSA infection rate and, subsequently, the length of hospital stay and the treatment costs (7, 8).

MRSA surveillance, in conjunction with an antibiotic care bundle (ACB) approach, has been recently proposed as a guide for correct treatment of patients admitted to ICU (9). ACB is a group of key elements based on clinical features and laboratory results for the management of antibiotic prescription. It ensures the use of the most effective drugs, leading to an intravenous versus oral switch or antibiotic de-escalation (8, 9). Several studies showed that rapid diagnostic tests to detect MRSA offer hope for early identification of positive patients, giving information to guide physicians about barrier precautions (7, 10). The introduction of various rapid molecular tests may improve infection control procedures, providing results within hours rather than days, as previously required by culture-based methods (11).

The aim of this study was to evaluate the risk of developing clinical MRSA infections in patients admitted to ICU who underwent MRSA surveillance by a polymerase chain reaction (PCR) nasal carriage screening test, with the purpose of suggesting a new specific ACB.
Patients and Methods

A group of 376 consecutive ICU adult patients were prospectively screened for nasal carriage of MRSA. There study group consisted of 244 (64.9%) males and (35.1%) females, with a median age of 64 (range 17-95 years). All swabs were obtained by inserting a Copan Liquid Stuart swab (Copan Diagnostics, Corona, CA, USA) in both nostrils. These were subsequently analyzed by GeneXpert MRSA (Cepheid, Sunnyvale, CA, USA) molecular test, able to amplify by real-time PCR the target sequence for MRSA at the SCCmec-orfX junction (12). The results were displayed on the Laboratory Information System and were subsequently available to ICU physicians within 2 hours from specimen receipt. All patients were followed-up during their ICU stay to determine whether they developed clinical MRSA infection, which was confirmed by a positive culture from sterile sites. Clinical samples from patients suspected of being MRSA-infected were tested by standard culture procedures.

The relative risk (RR) estimates and the associated 95% confidence interval (CI) was calculated and the Fisher exact probability test was used to compare categorical variables. The significance level was set at \( p<0.01 \).

Results

Overall, 26 (6.9%) patients were found to be MRSA-carrying, while 350 (93.1%) were MRSA-negative. No difference was observed in gender and age between these groups. During ICU stay, 9 (2.4%) patients developed generalized MRSA infection, of whom, 8 out of 26 (30.8%) were MRSA-carriers; one out of the 350 (0.3%) was MRSA-negative. Thus, a strong relationship between MRSA infection and MRSA carriage (RR=107.7, 95% CI 14.0-828.5, \( p<0.0001 \)) was found.

Among the eight patients with positive nasal screening who developed MRSA infection, four were symptomatic at admission to the ICU, while four patients acquired an MRSA infection during their ICU stay. Only one patient with negative nasal screening developed MRSA infection during his ICU stay. In any case, the finding of a MRSA-positive patient required immediate initiation of a correct antimicrobial treatment, according to the ACB reported in Table I.

Discussion

The real risk of developing MRSA colonization during the ICU stay is unclear, but MRSA positivity may result in increased morbidity and healthcare costs (6, 8). Recent studies suggested that the MRSA infection rate is always higher for MRSA-carriers and that nasal carriage of MRSA is strongly associated with the development of nosocomial infections, particularly among critically ill patients. Moreover, the risk of infection after MRSA colonization can be approximately 4-fold higher than the one of patients with methicillin-sensitive \( S. aureus \) (MSSA) colonization (5). In a prospective cohort study, nasal colonization with MRSA at ICU admission was the strongest independent predictor for subsequent MRSA infection (13). A recent multicentric prospective surveillance study confirmed a significant relationship between \( S. aureus \) colonization and invasive disease (6). Patients who have nasal carriage of MRSA upon ICU admission are significantly more likely to have MRSA bacteriemia compared with those without, with a prevalence ratio of 5.6 (14). An increased mortality rate among MRSA-
positive patients in respect to both MRSA-negative and MSSA-positive patients has been reported (3, 15). Several risk factors associated with MRSA infection have been suggested, such as age, chronic renal failure and concomitant bacterial infection (16). We found a significantly increased risk (RR=107.7, p<0.0001) of MRSA infection in patients with MRSA colonization, despite the relatively small population screened. Taken together, our results could underscore the importance of using the rapid molecular nasal screening for improving management and outcome of ICU patients. In fact, the real-time PCR assay is highly sensitive and quickly provides results to clinicians, leading to the better treatment of underlying infections (14).

The Institute for Health Improvement has defined as “bundle” a group of interventions related to a disease process which, when executed together, result in better outcomes than when implemented individually (17). ACB, already adopted in ICU as a method to optimize the management of sepsis or ventilator-associated pneumonia, has been demonstrated to achieve better outcomes by improving delivery of care (18). In particular, in recent years ACB has led to optimization of antibiotic management in critically ill patients (9, 19). We propose here a specific ACB, based on nasal colonization as a predictor of MRSA infection, which relies on clinical signs and laboratory results to trigger antibiotic treatment; hence a positive MRSA nasal screening result allows an empirical anti-MRSA coverage to be promptly implemented (Table I). The use of anti-MRSA agents is then re-evaluated daily on the basis of clinical and laboratory features, with positive cultures from sterile sites or signs of active infection supporting prolongation of empirical treatment. On the contrary, MRSA-negative clinical cultures support a de-escalation strategy.

In conclusion, the early identification of MRSA carriers using a rapid molecular screening is safe and accurate, allowing MRSA-positive patients who will more likely develop MRSA infections to be detected and managed appropriately. The suggested management of both MRSA-negative and MRSA-positive patients is reported in Figure 1.

References

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