Abstract. Aim: Colonization with methicillin-resistant Staphylococcus aureus (MRSA) is a risk factor for subsequent invasive MRSA infection, particularly in patients admitted to critical areas. We conducted a surveillance among patients admitted to our Intensive Care Unit (ICU) to determine whether the implementation of a specific MRSA antibiotic care bundle (ACB) based on rapid molecular screening for MRSA and decolonization, reduced the total MRSA infection rate. Materials and Methods: A total of 431 and 577 nasal swabs were obtained from ICU patients at admission from April 2009 through December 2010 (pre-ACB period) and, after the bundle implementation, from January 2011 through December 2012 (post-ACB period), respectively. Nasal swabs were analyzed by the rapid molecular test Xpert MRSA. All patients were followed-up during their whole ICU stay to determine whether they developed MRSA infection. Results: Overall, 31 out of 431 (7.1%) patients were colonized with MRSA at admission during the pre-ACB period and 49 out of 577 (8.4%) were colonized with MRSA during the post-ACB period. The rate of MRSA infection in ICU significantly declined from 2% in pre-ACB to 0.3% in post-ACB, with a total decrease of 100% in two consecutive semesters between July 2011 and July 2012 (p<0.001). Conclusion: The analysis demonstrated a significant decline in MRSA infections following the introduction of active rapid molecular surveillance and the specific ACB at our ICU and in the risk associated with MRSA bacteremia.

Colonization with methicillin-resistant Staphylococcus aureus (MRSA) is a risk factor for subsequent invasive MRSA infections, including ventilator-associated pneumonia, bacteremia and endocarditis, particularly in patients admitted to critical areas such as intensive care units (ICU) (1-3). Thus, MRSA-colonized patients should be closely monitored, being at higher risk as compared with non-colonized patients (4, 5). A rapid identification of MRSA nasal carriers is considered essential to limit the spread of resistant strains and to reduce MRSA infection rate and treatment costs (6-8). Recently published articles conclude that MRSA screening should be considered a useful tool for predicting in advance the etiology of the MRSA infection and for starting a correct empirical anti-microbial treatment (9, 10). Moreover, several studies demonstrated that MRSA colonization results must be rapidly delivered to critical care physicians to translate into an actual clinical impact, thus the recent introduction of rapid molecular tests can improve infection control procedures by providing results within hours rather than days (6, 7, 11). Furthermore, the centers for disease control and prevention (CDC) recommend that all healthcare organizations recognize previously-colonized patients, rapidly report MRSA laboratory results and consider active surveillance screening of patients to detect colonization even without evidence of infection, in order to prevent MRSA infection (12).

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 ICUs (13). ACB is a group of key elements based on clinical features and laboratory results for the management of antibiotic prescription (13, 14).

We conducted surveillance among patients admitted to our ICU and assessed the effects of implementation of specific MRSA ACB and prompt empirical anti-MRSA coverage, according to the ACB, on the prevalence of MRSA infection at our ICU.

Patients and Methods

A specific ACB was implemented in the period from January 2011 through December 2012 at our ICU and used as a guide for antibiotic treatment in patients suspected of being infected with MRSA. The bundle consisted of rapid molecular screening for
MRSA nasal carriage, contact precautions, single room or cohort isolation, and nasal decolonization (mupirocin 2% ointment three times-a-day for five days) for patients colonized or infected with MRSA (15). At admission, we collected specimens from sterile sites for bacterial culture prior to antibiotic administration and took nasal swabs for rapid MRSA screening. A total of 431 and 577 nasal screening tests were obtained from April 2009 through December 2010 (pre-ACB period) and from January 2011 through December 2012 (post-ACB period) from patients admitted to our ICU. In cases of positive nasal carriage and suspected bloodstream infection, first-line empirical anti-MRSA treatment with vancomycin, 15 mg/kg loading dose, followed by 30 mg/kg/day continuous infusion was used. All patients were followed-up during their ICU stay to determine whether they developed clinical MRSA infection, confirmed by a positive culture from sterile sites. The use of anti-MRSA agents was then re-evaluated day by day on the basis of clinical and laboratory features, with positive cultures from sterile site or signs of active infection supporting prolongation of empirical treatment (15). On the contrary, MRSA-negative clinical cultures indicated a de-escalation strategy.

All nasal swabs were obtained by inserting a Copan Stuart swab (Copan Diagnostics, Corona, CA, USA) in both nostrils and analyzed using the molecular test Xpert MRSA (Cepheid, Sunnyvale, CA, USA). The results of rapid nasal screening were displayed on the Laboratory Information System and subsequently available to ICU physicians within 2 h from specimen receipt. Clinical samples from patients suspected as being infected with MRSA were tested by standard laboratory culture procedures. Comparisons of relative risk reduction (RRR), relative risk (RR) and the associated 95% confidence interval (CI) between the two study periods were performed using Fisher’s exact test. The significance level was set at $p<0.02$.

**Results**

Overall, 31 out of 431 (7.1%) patients were colonized with MRSA at admission during the pre-ACB period while 49 out of 577 (8.4%) were colonized with MRSA during the post-ACB period. All colonized patients in the post-ACB period (49 of 577) were de-colonized at admission with mupirocin ointment. During the pre-ACB period 9 patients developed generalized MRSA infection, compared with only two cases in the post-ACB period. The total rate of MRSA infection during the pre-ACB period was 2% (20.8 per 1,000 admissions) but reduced to 0.3% (3.4 per 1,000 admissions) in the post-ACB period, with a total decrease of 100% in two consecutive periods between July 2011 and July 2012 ($p<0.001$). The rate of MRSA infection among positive nasal carriers dropped from 30% in the pre-ACB period to 4% in the post-ACB period although the nasal MRSA colonization rate at admission increased respectively from 7.1% to 8.4%.

The statistical analysis shows the RR and RRR after interventions were 0.14 (95%CI=0.02-0.63) and 0.85 (95% CI=0.36-0.97; $p=0.002$) respectively. Overall, during the two study periods, low respiratory tract (LRTI) and bacteremia infections were most frequent (78%) but significantly declined after ACB [seven cases (1.6%) in the pre-ACB period vs. only one case (0.2%) in the post-ACB period] with a RRR of 91%. Moreover, the RRR of bacteremia infection alone in the post-ACB period was 100% ($p=0.02$) (Table I).

**Discussion**

In the present study we demonstrated that implementation of a specific ACB at admission significantly reduced the MRSA infection prevalence at our ICU, from 20.8 per 1,000 admissions to 3.4 per 1,000 admissions. The statistical analysis showed a significant reduction of the risk of MRSA infections among colonized patients managed following the ACB protocol and in particular of the risk associated with MRSA bacteremia (RRR 100%, $p=0.02$).

In a recently published study, we found a significantly increased risk of MRSA infection in ICU patients with MRSA colonization compared with patients without (15), in line with recent reports which suggested that MRSA infection rate is always higher for MRSA carriers and that MRSA nasal carriage is strongly associated with development of nosocomial infections, particularly among critically ill patients (4, 16). Furthermore, MRSA infections are associated with worse outcomes and a substantial increase in healthcare costs compared to sensitive infections (17). To date, the benefit of earlier screening of MRSA nasal carriers as a strategy to reduce the MRSA infection rate is debated and several recent studies have shown discordant results (18-20). However, in many studies, the authors used traditional culture methods instead of polymerase-chain-reaction, reducing the sensitivity of the analysis, and even when they used molecular methods, identification and decolonization of nasal carriers was not immediate after admission, or the sample processing frequency and the reporting time were not satisfactory (18, 21).

Chan et al. in a recently published article highlight the usefulness of active surveillance culture as a predictor of MRSA ventilator-associated pneumonia (9). In the same journal, Toschlog et al. posed several interesting issues on the study by Chan and colleagues related to the low sensitivity of selective agars used as screening method (11 patients developed MRSA ventilator-associated pneumonia with negative screening cultures) and to what the impact on the screening performance would have been if a PCR method had been used instead of cultures (10).

In a recent randomized, multicenter trial (22), rapid identification of *S. aureus* nasal carriers by a PCR assay, followed by de-colonization reduced the risk of nosocomial *S. aureus* infection by nearly 60%. In their study, in contrast with previous randomized trials, nasal carriage of *S. aureus* was detected rapidly by real-time PCR at the time of hospital admission. On the contrary, Huskins and colleagues in a recent cluster-randomized trial had different results, showing no effect on reducing the trasmission of MRSA after the
intervention (20). In their study, several factors may have influenced the effects of the intervention, but the average time from when a surveillance culture was obtained until the reporting time to clinicians of five days, surely limited the efficacy of surveillance (23).

In a recently point–counterpoint article, Peterson reports a summary of published studies that show how the level of test sensitivity and reporting time of results modify the reduction of MRSA infection. For each of these studies Peterson calculated the percentage of captured potential MRSA isolation days based on level of test sensitivity, reporting time and length of hospital stay. Interestingly, in those reports, a reduction of MRSA transmission or infection during the intervention periods was achieved only when the estimated captured MRSA isolation days exceeded 80%, which implies that the assay sensitivity and a rapid reporting time are critical to the outcome. On the contrary, in the same article Diekema highlighted that in some studies other infection control strategies, such as hand hygiene or chlorhexidine body washes for all ICU patients, may be more effective in reducing the incidence of MRSA, rather than rapid screening tests (18).

In our study, we detected MRSA carriage immediately after admission, by a rapid PCR method, with results being reported within two hours, factors that certainly improved the efficacy of our intervention. Although the cost associated with the PCR-based assay is substantially more expensive, this screening method is sensitive and capable of providing results within 2-3 h, significantly shorter than cultures. It allows MRSA-positive ICU patients who will more likely develop MRSA infections to be rapidly detected and managed appropriately, not only by guiding empirical therapy decisions but also by implementing meaningful measures to limit the person-to-person transmission (24). Some believe it is preferable to use active surveillance cultures instead of PCR to improve cost-effectiveness. However, other investigators believe that restricting molecular screening for MRSA to high-risk patients, such as those admitted to ICU, could be a cost-effective strategy to reduce infection rates and transmission of MRSA (25, 26). In conclusion, although more randomized controlled trials are needed to determine the potential impact of our approach on patient outcomes, our results underscore the importance of using active surveillance for improving management and outcome of ICU patients. However, we believe that the impact is strictly dependent on the sensitivity of the test used, initiation of MRSA nasal screening, de-colonization immediately after admission, and rapid reporting.

References


