MEDICAL VALUE OF RAPID MRSA/SA SCREENING IN EMERGENCY SURGERY

ANNE DUBOUIX-BOURANDY, LABORATORY MANAGER AND HEAD OF MICROBIOLOGY, CLINIQUE DE L'UNION, FRANCE

This article looks at the impact of *Staphylococcus aureus* on patients and shows how it can lead to greater cost burdens and longer stays in hospital. One of the ways that the risk of hospital-acquired infections can be reduced is through screening patients for MRSA before treatment. In the past, screening has led to delays in treatment regimens and unnecessary isolation for patients awaiting the results. New molecular diagnostic tests offer faster results and can produce a significant decrease of *Staphylococcus aureus*-associated hospital-acquired infections in emergency settings.

Staphylococcus aureus and hospital-acquired infections

Staphylococcus aureus is a common microorganism which can be present without any infection in many body sites such as nostrils, throat and skin. *Staphylococcus aureus* nasal carriage ranges from 20% to 50% depending on the considered population and the country *(1)*. Furthermore, *Staphylococcus aureus* can be easily transmitted by cross-transmission between people but also during medical procedures or through the environment. In the last decades, this bacterium has become progressively resistant to betalactams because of the extended use of this antibiotic class. This is a major issue as resistance to methicillin in *Staphylococcus aureus* (MRSA) is frequently associated with other antibiotic resistances. In this case, glycopeptids often remain the only therapeutic option. This contributes to unfavorable antibiotic prescription and increases the selection pressure on other species (aka enterococci for example).

In the United States, the prevalence of MRSA among clinical *Staphylococcus aureus* isolates is over 53% *(2)*, while in countries where a strict nationwide infection control policy is conducted, such as northern Europe, the prevalence in the species is around 1% *(3)*. When the immune system is compromised or skin barrier disrupted because of surgery or invasive procedures (intravascular devices, for example), *Staphylococcus aureus* can spread into the organism and be responsible for hospital-acquired infections (HAI).

According to CDC data, *Staphylococcus aureus* is the second most prominent bacterium reported by the National Healthcare Safety Network. It represents 14% of HAI and is mainly responsible for surgical site infections (30%), ventilator-associated pneumonia (24%) and bacteremia. In this case too, methicillin resistance is a growing threat as 49% to 65% of HAI reported to NHSN are caused by MRSA *(4)*.

This resistance is even more worrying in Asia where 82% of the *Staphylococcus aureus* strains isolated in hospital-acquired pneumonia or bacteremia are MRSA *(5)*.

Hospital acquired infections caused by MRSA have been associated with increased mortality. Higher mortality rates can be observed for MRSA bacteremia, hospital-acquired pneumonia and surgical site infections (SSI). Engeman et al. demonstrated that patients developing a MRSA SSI had a greater 90-day mortality rate than did patients infected with methicillin-susceptible *S. aureus (6)*. This is probably due to a higher expression of virulence factors, but also to comorbidities such as age, gender, severity of the illness and time to receive the right antibiotic therapy.

More than 80% of *Staphylococcus aureus* HAIs are endogenous and are linked to the carrier status. Indeed, it has been clearly demonstrated that nasal carriers of *Staphylococcus aureus* have a risk of HAI with this microorganism which is two to nine times higher than the risk among non-carriers *(7)*.

Infections with *Staphylococcus aureus* cause heavy financial burdens on healthcare systems worldwide

Methicillin-resistant *Staphylococcus aureus* (MRSA) HAIs are associated with higher healthcare costs *(8)*. The main cost drivers are prolongation of hospital stay due to higher morbidity and implementation of contact precaution measures (gowns, gloves, isolation in single room, etc). Engeman demonstrated that patients infected with MRSA had an average of five additional days with respect to patients infected with

methicillin-susceptible *Staphylococcus aureus*. Furthermore, it is interesting to note that median hospital charges were US$ 29,455 for non-infected patients, US$ 52,791 for patients infected with methicillin-susceptible *Staphylococcus aureus* and US$ 92,363 for patients suffering from MRSA surgical site infection. MRSA surgical site infections can be associated with a 1.19-fold increase in the median hospital cost and an additional US$ 13,901 mean cost per case for patients with methicillin-susceptible *Staphylococcus aureus* surgical site infections *(6)*.

Staphylococcus aureus screening and decolonization: The screen-and-treat strategy

As mentioned previously, the risk of developing a *Staphylococcus aureus* HAI is related to the *Staphylococcus aureus* carriage. Many studies have pointed out the value of screening such patients.

Screening consists of searching for the presence of *Staphylococcus aureus* in the nose/throat and skin of the patients and to decolonize them with a combination of mupirocin nasal ointment and chlorhexidine bathing in order to eradicate the bacterium.

In a recent clinical trial that assessed the effect of nasal mupirocin treatment in surgical patients who were *Staphylococcus aureus* carriers, the eradication of *Staphylococcus aureus* resulted in a 60% decrease of the rate of HAIs with this pathogen *(9)*. Similar results, as well as an impact on the duration of hospitalization, were also found by Hubner et al *(10)*.

Furthermore, Bode and colleagues were recently able to demonstrate that detection and decolonization of *Staphylococcus aureus* carriage not only prevents *Staphylococcus aureus* surgical site infections, but also reduces a 1-year mortality in surgical patients undergoing clean procedures *(11)*.

Interestingly, when medical costs are evaluated, similar findings are also observed. Recently, Van Rijen et al. compared a population screened and decolonized versus a control population and showed that if a screen-and-treat strategy was adopted, the cost of care in the decolonized group was on average €1,911 lower than the cost of care in the control group. Indeed, decolonized cardiothoracic patient hospitalization cost €2,841 less than in the control group while decolonized orthopaedic patients' hospitalization cost €955 less than the non-treated patients *(12)*.

Staphylococcus aureus screening and medical value

The screen-and-treat option is the key to a global infection control strategy, however, it is also related to additional costs, such as extra laboratory costs, pre-emptive isolation of the patients in single rooms, nursing costs, housekeeping costs, etc. It is, though, a strategy up for discussion and is not universal (systematic screening and decolonization of all patients) but must be displayed in settings where it can add a real medical value (cardiothoracic surgery, orthopaedics and traumatology, ICU, etc). Indeed, patients with a high risk of developing SA infections (those exhibiting specific risk factors such as age, poor general condition, or undergoing certain kinds of surgery) should therefore be the primary target when implementing this strategy in clinical practice.

Until a few years ago, screening was mostly based on conventional microbiology culture. This method has to address two important issues: standard culture displays a diagnostic delay of three to five days which increases the isolation burden and does not allow screening in all circumstances (for example, in emergency surgery). Furthermore, it needs experienced staff to perform it and can be limited by laboratory opening hours.

It is interesting to note that the vast majority of patients considered at risk for carriage will not be colonized with MRSA, yielding considerable amounts of unnecessary isolation days as isolation measures are costly and may compromise the quality of patient care *(13)*.

Additionally, patients exhibiting a high risk of MRSA carriage, for example, elderly patients frequently undergo emergency surgery (such as hip fractures, hip replacement) and therefore can not be screened with the conventional culture method in these circumstances. This can be considered as a real lost chance, considering the increased prevalence of MRSA in this population.

A solution to this situation relies on the rapid diagnostic testing that has dramatically evolved in the last decade. Indeed, several companies have understood the crucial interest of being able to provide hospitals with easy-to-use assays providing a very short time to a result in order to help healthcare providers to manage effectively the infection control strategy. These assays are based on the simultaneous molecular detection of several bacterial genes (detecting simultaneously *Staphylococcus aureus* carriage and methicillin resistance) directly from patients' samples. They are simple enough to be carried out by trained professionals without extensive technical skills and are compatible with point-of-care activity. They can thus be performed 24/7 and promote a universal access to screening for high-risk populations even in emergency settings. Time to result can be as quick as one hour, allowing a multidisciplinary bundle involving a rapid decontamination, an implementation of isolation measures, if needed, and an adapted antibiotic prophylaxis before the surgery *(10, 13)*.

For years routine implementation of molecular-based screening tests was limited by their high cost (they are actually

three to four times more expensive than culture-based methods). Interestingly, many authors decided to focus on the medical value of the implementation of such assays in the prevention and the control of *Staphylococcus aureus* HAIs. It is now admitted that even if the test itself is more expensive, the medical value added is clearly non-neglectable *(13)*.

Boostma et al. demonstrated that culture methods are insufficient to control MRSA and that rapid diagnostic testing could lead to a 90% decrease of in isolation needs when used *(14)*. In the same way, Wassemberg et al. demonstrated a significant reduction of isolation (96 hours for culture versus 21.4 hours with molecular screening) leading to discontinuation of pre-emptive isolation in 62.6% of the ICU patients *(13)*.

Bode et al., put in evidence that the preventive effect of *Staphylococcus aureus* decolonization was associated with a reduced risk of *Staphylococcus aureus* HAIs by nearly 60% *(9)*. They also demonstrated that as nasal carriage of SA was rapidly detected by means of PCR at the time of hospital admission, the rapidity of this assay contributed significantly to the outcome. Indeed, it allowed targeted decolonization treatment to be initiated within 24 hours of admission – that is before patients have been exposed to risk factors for *Staphylococcus aureus* HAIs *(11)*.

Conclusion

It is now acknowledged that screening *S Staphylococcus aureus* carriers and decolonization of the patients leads to significant a decrease of *Staphylococcus aureus* associated hospital-acquired infections in certain settings: cardiosurgery, orthopaedics and traumatology. It is also associated with a decrease in the morbidity and the mortality of these patients, which has an impact on the length of hospitalization and the hospital costs.

This strategy is easy to carry out, however, it can be limited by time-to-result in emergency settings where patients are at high risk of *Staphylococcus aureus* carriage. A solution relies on molecular testing. PCR-based methods have a time-to-result of a few hours, which allows the implementation of a multidisciplinary bundle. They are associated with a reduction of surgical site infection and length of stay, as well as a decrease in the number of unnecessary isolation days and the costs, even if the technique by itself is more expensive than conventional culture. ■

Dr Anne Dubouix-Bourandy is an expert in medical microbiology and infection control. She obtained post-graduate degrees in clinical pathology, medical microbiology and infection control as well as a PhD in molecular pathophysiology from Toulouse University. She pursued her post-doctoral research as a Harvard fellow and has served as Associate Professor of Clinical Microbiology and Hospital Practioner at Toulouse's University Hospital. She is currently Laboratory Manager and Head of Microbiology at Clinique de L'Union.

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