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Opinion

Reducing the Uncertainty of the Empirical Treatment of Hospital Acquired (HAP) and Ventilator Associated Pneumonia (VAP) against MSSA/MRSA is Feasible

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Hospital-acquired pneumonia (HAP) is defined as pneumonia that occurs ≥48 hours after hospital admission, while ventilator-associated pneumonia (VAP) develops more than 48 hours after the initiation of mechanical ventilation [1].

Both entities might be considered as an unfavorable result of the medical care and should be prevented. Several prevention guidelines, particularly in the case of VAP, have been implemented throughout the last few years in Spain showing their effectiveness [2]. Nevertheless, not all countries follow the same recommendations and even doing so some patients will suffer HAP/VAP.

Once HAP/VAP are clinically suspected the attending physician must balance between starting wide spectrum antibiotics as soon as possible and limiting unnecessary coverage because delaying the correct antibiotic against the causative pathogen has been associated with higher mortality rate [3] but using superfluous antibiotics increases the risk of adverse events, super infections, and antimicrobial resistance [4].

The main microorganisms causing HAP/VAP can vary highly depending on different countries [5,6] and even amongst different hospitals within the same country [7] so a standard empirical treatment cannot be recommended. One of the most controversial issues is knowing when methicillin-susceptible (MSSA) and particularly methicillin-resistant *Staphylococcus aureus* (MRSA) should be empirically treated. There are two main recommendations to start empiric treatment against MSSA/MRSA, one of them is based on the prevalence of MRSA in the hospital or Intensive Care Units (ICU) and the other one on the existence of risk factors. Recent published IDSA guidelines [1] suggest that in those ICU with prevalence rates of >10% – 20% of MRSA a gram-positive agent active against MRSA should be given. On the other hand, well-established individual risk factors of each patient, such as comorbidity, prior exposure to antibiotics and the presence of shock [8,9] should always be considered before prescribing the treatment. Nevertheless, this strategy of starting anti-MRSA treatment based on these two principles has important limitations because MRSA has shown to produce the same rate of early VAP in patients without risk factors (15.8%) than late VAP (17.4%) in some studies [10].

All these circumstances lead the clinician to choose an empiric anti-MRSA antibiotic, probably many more times than the patients need increasing the toxicity and costs but paradoxically this strategy does not guarantee that all the infected patients by MRSA receive the correct antibiotic from the beginning.

Different rapid real-time polymerase chain reaction (PCR) methods have been developed over the last few years for detection of MSSA/MRSA at the bedside [11].

The Xpert MRSA/SA SSTI™, Cepheid, Sunnyvale, CA PCR assay for automated simultaneous detection of MSSA and MRSA in samples of skin and soft tissue infection swabs and blood [12] has been approved by the Food and Drug Administration (FDA) and European

Community (CE). This test is based on the simultaneous amplification of three gene targets (spa, mecA, and staphylococcal cassette chromosome mec element [SCCmec]) and on fluorogenic target-specific hybridization probes for the detection of the amplified DNA. The random-access Xpert performs extraction, amplification, and detection of the targets in a single-use cartridge. Results are reported within 60 minutes either as "MSSA" if only spa is amplified, as "MRSA" if spa, mec gene and SCCmec are simultaneously detected, or as "negative" if none of these is found. Off-label use of the assay for the detection of MSSA/MRSA in lower respiratory tract secretions has been evaluated by several authors and demonstrated to have high sensitivity and specificity. It is particularly important that its negative predictive value nearly 100% [13-16] would allow the clinician to avoid unnecessary MSSA/MRSA coverage to those patients with a negative test. This new technology will facilitate to put in practice the concept of personalized medicine. Clinicians will treat each patient with the best antibiotic from the beginning saving unnecessary treatments. Of course, this test does not substitute the work of the microbiologist and the conventional culture should be done to guarantee the performance of the test and to isolate the causing microorganism. In addition, as the performance of conventional culture has some false negative results, using this test when suspecting HAP/VAP might have another potential advantage because a small proportion of patients without risk factors who are unlikely to be empirically treated against MSSA/MRSA might be positive for the test benefitting from early specific antibiotic treatment. Although perhaps irrelevant from an epidemiological perspective, starting antibiotic against MSSA/MRSA two or three days before the isolation of MSSA/MRSA in culture could improve the outcome of a few patients.

I consider that a good strategy to reduce unnecessary treatment anti-MSSA/MRSA minimizing risks of not treating soon enough real infections requires to implement these rapid tests in a daily basis when HAP/VAP is suspected to individualize the best antibiotic from the beginning.

Bibliography

1. Kalil AC., *et al*. "Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society". *Clinical Infectious Diseases* 63.5 (2016): e61-e111.

2. Álvarez Lerma F., *et al*. "Guidelines for the prevention of ventilator-associated pneumonia and their implementation. The Spanish "Zero-VAP" bundle". *Medicina Intensiva* 38.4 (2014): 226-236.

3. Dupont H., *et al*. "Impact of appropriateness of initial antibiotic therapy on the outcome of ventilator-associated pneumonia". *Intensive Care Medicine* 27.2 (2001): 355-362.

4. Monroe S and Polk R. "Antimicrobial use and bacterial resistance". *Current Opinion in Microbiology* 3.5 (2000): 496-501.

5. Rello J., *et al*. "Differences in hospital- and ventilator-associated pneumonia due to Staphylococcus aureus (methicillin-susceptible and methicillin-resistant) between Europe and Latin America: a comparison of the EUVAP and LATINVAP study cohorts". *Medicina Intensiva* 37.4 (2013): 241-247.

6. Herkel T., *et al*. "Epidemiology of hospital-acquired pneumonia: Results of a Central European multicenter, prospective, observational study compared with data from the European region". *Biomedical papers of the Medical Faculty of the University Palacký, Olomouc, Czechoslovakia Repub* 160.3 (2016): 448-455.

7. Olaechea PM., *et al*. "Characteristics and outcomes of patients admitted to Spanish ICU: A prospective observational study from the ENVIN-HELICS registry (2006-2011)". *Medicina Intensiva* 40.4 (2016): 216-229.

8. Bouza E., *et al*. "Ventilator-associated pneumonia due to meticillin-resistant Staphylococcus aureus: risk factors and outcome in a large general hospital". *Journal of Hospital Infection* 80.2 (2012): 150-155.

9. Wooten DA and Winston LG. "Risk factors for methicillin-resistant Staphylococcus aureus in patients with community-onset and hospital-onset pneumonia". *Respiratory Medicine* 107.8 (2013): 1266-1270.

10. Martin-Loeches I., *et al*. "Potentially resistant microorganisms in intubated patients with hospital-acquired pneumonia: the interaction of ecology, shock and risk factors". *Intensive Care Medicine* 39.4 (2013): 672-681.

11. Lepainteur M., *et al*. "Comparative Evaluation of Two PCR-Based Methods for Detection of Methicillin-Resistant Staphylococcus aureus (MRSA): Xpert MRSA Gen 3 and BD-Max MRSA XT". *Journal of Clinical Microbiology* 53.6 (2015): 1955-1958.

12. Wolk DM., *et al*. "Rapid detection of Staphylococcus aureus and methicillin-resistant S. aureus (MRSA) in wound specimens and blood cultures: multicenter preclinical evaluation of the Cepheid Xpert MRSA/SA skin and soft tissue and blood culture assays". *Journal of Clinical Microbiology* 47.3 (2009): 823-826.

13. Cercenado E., *et al*. "Rapid detection of Staphylococcus aureus in lower respiratory tract secretions from patients with suspected ventilator-associated pneumonia: evaluation of the Cepheid Xpert MRSA/SA SSTI assay". *Journal of Clinical Microbiology* 50.12 (2012): 4095-4097.

14. Leone M., *et al*. "Routine use of Staphylococcus aureus rapid diagnostic test in patients with suspected ventilator-associated pneumonia". *Critical Care* 17.4 (2013): R170.

15. Oh AC., *et al*. "Clinical utility of the Xpert MRSA assay for early detection of methicillin-resistant Staphylococcus aureus". *Molecular Medicine Reports* 7.1 (2013): 11-15.

16. Velasco López E., *et al*. "Utility of a Multiple Real-Time PCR Assay for Choice of Empirical Antibiotics in VAP". *Intensive Care Medicine* 39.2 (2013): 382.

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