Editorial

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Not all nosocomial pneumonias are the same

No todas las neumonías nosocomiales son iguales

Nem todas as pneumonias nosocomiais são iguais

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Nosocomial pneumonia, the most widespread and deadly of all acute diseases, called the captain of death according to Sir William Osler, continues to be a major problem in hospital medicine, both due to its frequency and the high mortality with which it is associated. In North America it is among the ten most frequent causes of death in all age groups and is the leading cause of death from infection, with crude mortality between 20 and 50%. A third part is acquired in the ICU, 90% related to mechanical ventilation.

It is also produced by a great variety and an increasing number of microorganisms. As if this were not enough, there is usually a significant difficulty in establishing a specific etiological and clinical diagnosis, while multiple antimicrobial regimens are currently available. All this in a historical moment of a high, growing and worrying prevalence of resistance to antibiotics, to which is added another not insignificant factor such as the wide diversity of medical specialties involved in the daily management of this problem and that in some way makes it more difficult to standardize criteria and create consensus, make it a must. Many current voices point to the imminent problem of the growing post-pandemic multi-resistance to antibiotics, a situation that is certainly of great concern; multidrug-resistant bacteria are associated with higher mortality, especially Gram negative germs such as *Pseudomonas aeruginosa*, *Acinetobacter* and *Enterobacteraceae*. In the ICU, multidrug-resistant pathogens are equally important and are associated with a high risk of adverse outcomes; at least between 20 and 30% of *Pseudomonas aeruginosa* ventilator-associated pneumonias (VAP) correspond to multiresistant strains. A recent multicentric cohort study showed in a group of almost 4,000 patients, a higher incidence of VAP occurring among coronavirus disease-19 patients compared with the general ICU population (25.5; 95% CI [23.7-27.45] vs 15.4; 95% CI [13.7-17.3] per 1,000 ventilation days), with a similar microbiological ecology and resistance pattern, with a predominance of *Enterobacterales* and nonfermenting Gram-negative bacteria.

The critically ill patient, on the other hand, has complex pharmacokinetic and pharmacodynamic profiles that make this problem harder.

These facts give relevance to nosocomial pneumonia today, since it constitutes a global public health problem, however is it valid to ask ourselves if all nosocomial pneumonias are the same? Maybe not.

The categories of pneumonia by clinical scenario traditionally considered include community-acquired pneumonia, pneumonia of the elderly, nosocomial pneumonia, pneumonia of the immunocompromised host, and those related to cystic fibrosis and anatomical abnormalities. Within the nosocomial group, hospital-acquired pneumonia and ventilator-associated pneumonia are included, the concept of healthcare-associated pneumonia having been abandoned for not making a clear distinction between a particular population; most of the available evidence and information comes from the VAP. The concept of ventilated nosocomial pneumonia has recently been introduced by some authors, and importantly, it has been pointed out that mortality from all causes associated with this new category is definitely higher (27.8%) than that of the same VAP (18%) and hospital-acquired pneumonia (14.5%), which gives strength to this concept and suggests that it is indeed a different category of nosocomial pneumonia. These patients are generally admitted to the general floor, being both medical and surgical cases that are complicated, integrating the diagnosis of nosocomial pneumonia in the traditional way, after which they take a bad clinical course, evolving towards acute respiratory failure, not responding to oxygen and standard initial management, having to be intubated and transferred to the ICU to be mechanically ventilated. A few will be in the ICU, coronary unit or a stepdown unit without any ventilatory support and will similarly be complicated by severe acute respiratory failure associated with pneumonia and will need to be intubated. This is not unknown to the community of intensive care physicians, however its high mortality had been overlooked.

Different database series have documented this high mortality, although it should be noted that all except one have links with the pharmaceutical industry, which does not invalidate them, but does make it necessary to take these data with caution.

In these series, mortality from recently reported ventilated hospital-acquired pneumonia ranges from

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6.5 to 24% at 14 days and 15.2 to 39.4% at 28 days vs 6.3 to 19.8% and 10.2 to 27% for VAP in the same periods (3.1 to 17.4% and 9.8 to 18.8% for standard non-ventilated hospital-acquired pneumonia). There is an independent series, reported by researchers from the University of Barcelona and that we can consider free of any bias that describes the same phenomenon. All-cause mortality in patients with ventilated hospital-acquired pneumonia was 14.4% (95% CI 7.7, 21.2) at 7 days, 24% (95% CI 15.8, 32.3) at 14 days, 28.8% (95% CI 20.1, 37.6) at 21 days, 39.5% (95% CI 30.0, 48.8) at 28 days and 47.1% (95% CI 37.5, 56.7) at 90 days, figures much higher than those observed in VAP (9.3, 19.8, 25.4, 27 and 36.7%) in the same periods and in the traditional form (non-ventilated) of hospital-acquired pneumonia (11.6, 17.4, 20.3, 21.7 and 30.4%), respectively.

Minor criteria for severe hospital-acquired pneumonia have been suggested, including tachypnea, PaO_2/FiO_2 ratio < 250, multilobar pulmonary infiltrates, confusion, disorientation, uremia, leukopenia, thrombocytopenia, hypothermia, as well as hypotension requiring fluid loads, as well as major criteria among which are the need for non-invasive mechanical ventilation and septic shock with the need for vasopressors. And although there are a multitude of different diagnostic and therapeutic approaches, it is advisable to rely on the best available evidence through the implementation of existing guidelines, updated and published by different collegiate bodies in the world. One of the most representative are those of the Infectious Diseases Society of America and the American Thoracic Society (IDSA/ATS), the latest version of which is turning five years old, which includes levels of recommendation and quality of evidence on practical aspects of diagnostic sampling, initial empirical management (covering the possibilities of *Staphylococcus aureus*, *Pseudomonas aeruginosa* and other Gram negative bacilli), highlighting the importance of local infection committees, ideally specific to each ICU, from which the knowledge of the actual microbiology of each unit is derived. It also highlights the need of adapting the empirical choice of antibiotics based on knowledge of the risk factors for antimicrobial resistance in each case (highlighting the use of antibiotics in the previous 90 days), as well as the percentage of resistant Gram negative isolates in each ICU, and the percentage isolation of methicillin-resistant *Staphyloccocus aureus*.

Whether or not we have a new category of hospital-acquired pneumonia remains to be seen, we need new multicenter prospective series, more data, better information, but in the meantime we must remember the importance of hospital-acquired pneumonia and recognize all the important variables it affects, as well as perform the best planning to address this problem locally in the best possible way, ensuring the appropriate use of antibiotics, adhering to the guidelines in a contextualized manner and being attentive to advances in the matter.

Finally, I want to remind you that there are many non-infectious causes of a febrile pneumonitis syndrome and many non-cytotoxic drugs capable of simulating a pulmonary infection, factors to remember in non-responsive pneumonia. Certainly pneumonia of any kind continues to be a challenge for the clinician, and even more so for the intensive care physician.

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