Update on infections in ICU patients

Francisco Álvarez-Lerma[a], Jesús Rodríguez-Baño[b], Jordi Solé-Violán[c], Luis Álvarez-Rocha[d], Rosario Menéndez[e], Marcio Borges[f], Pedro Olaechea[g], Rafael Zaragoza[h], José Garnacho-Montero[i], Pilar Luque[j], Cristóbal León[k], Óscar Rodríguez[l], Antoni Torres[m] Julián Álvarez[n], Mercedes Nieto[o] and Leonardo Lorente[p]

[a]Servicio de Medicina Intensiva. Hospital del Mar. Barcelona. Spain. [b]Sección de Enfermedades Infecciosas. Hospital Universitario Virgen Macarena. Sevilla. Spain. [c]Servicio de Medicina Intensiva. Hospital Universitario de Gran Canaria Dr. Negrin. Las Palmas de Gran Canaria. Spain. [d]Servicio de Medicina Intensiva. Hospital Juan Canalejo. A Coruña. Spain. [e]Servicio de Neumología. Hospital Universitario La Fe. Valencia. Spain. [f]Servicio de Medicina Intensiva. Hospital Son Llàtzer. Palma de Mallorca. Spain. [g]Servicio de Medicina Intensiva. Hospital de Galdakao. Vizcaya. Spain. [h]Servicio de Medicina Intensiva. Hospital Dr. Peset. Valencia. Spain. [i]Servicio de Medicina Intensiva. Hospitales Universitarios Virgen del Rocío. Sevilla. Spain. [j]Servicio de Medicina Intensiva. Hospital Clínico Universitario. Zaragoza. Spain. [k]Servicio de Medicina Intensiva. Hospital Universitario de Valme. Sevilla. Spain. [l]Servicio de Medicina Intensiva. Hospital Clínico Universitario. Valencia. Spain. [m]Servicio de Neumología. Instituto Clínico del Tórax. Hospital Clínic. Barcelona. Spain. [n]Servicio de Anestesia, Reanimación y Terapia del Dolor. Hospital Clínico Universitario de Santiago de Compostela. A Coruña. Spain. [o]Servicio de Medicina Intensiva. Hospital Infantil Universitario Niño Jesús. Madrid. Spain. [p]Servicio de Medicina Intensiva. Hospital Universitario de Canarias. La Laguna. Tenerife. Spain.

Studies carried out in 2006 on severe community-acquired pneumonia or nosocomial pneumonia requiring admission to the ICU are numerous and of a high quality. Among studies of community-acquired pneumonia, the most relevant are those focused on the development and evaluation of systems for the identification of patients with severe pneumonia, analysis of the impact of the initial inflammatory response on the course of the disease, and level of adherence to therapeutic guidelines proposed by different scientific societies. Among studies of nosocomial pneumonia, those involving ventilator-associated pneumonia and health care-associated pneumonia should be emphasized. The reliability of different respiratory sampling methods for the etiological diagnosis of pneumonia, the impact of different etiological agents, and the efficacy of prophylactic measures have been the object of different investigations. Important aspects of these studies include the assessment of different strategies in the use of antimicrobial agents to decrease the selection of multiresistant pathogens. Moreover, early identification of patients at risk of invasive fungal infections, as well as preemptive treatment of these infections in selected patients have been topics of increasing interest.

Key words: **Infections. ICU. Update.**

Actualización sobre infecciones en pacientes de la UCI

Los estudios realizados en 2006 sobre la neumonía extrahospitalaria grave o la neumonía nosocomial que requieren el ingreso en la UCI son numerosos y de gran calidad. Entre los trabajos sobre la neumonía extrahospitalaria, los más relevantes son los que se basan en el desarrollo y la valoración de los sistemas para identificar a los pacientes con neumonía grave, en el análisis del impacto de la respuesta inflamatoria inicial sobre el curso de la enfermedad, y en el nivel de seguimiento de las normas terapéuticas propuestas por diferentes sociedades científicas. Entre los estudios sobre la neumonía nosocomial, cabe destacar los relacionados con la neumonía asociada al respirador o a la asistencia sanitaria. La fiabilidad de los distintos métodos para obtener muestras respiratorias con el fin de establecer el diagnóstico etiológico, el impacto de los diferentes agentes etiológicos, y la eficacia de las medidas profilácticas, han sido objeto de diversas investigaciones. Entre los aspectos importantes de estos estudios se halla la valoración de las diferentes estrategias para el uso de los agentes antimicrobianos con el fin de reducir la selección de los gérmenes plurirresistentes. Además, la identificación precoz de los pacientes con riesgo de infecciones micóticas invasivas, así como el tratamiento precoz de estas infecciones en determinados pacientes, han sido otros tantos temas de interés general.

Palabras clave: **Infecciones. UCI. Actualización.**

State of the art

In 2006, many studies on community- and nosocomially-acquired infections affecting critically ill patients[1-27] were published. Their objective was to improve the clinical management of patients with infections in order to reduce

Correspondence: Dr. F. Álvarez-Lerma.
Servicio de Medicina Intensiva.
Hospital del Mar.
Pg. Marítim, 25-29. 08003 Barcelona. Spain.
E-mail: falvarez@imas.imim.es

infection-related mortality and morbidity. All of the studies focus on the following: *a)* designing strategies for early identification of patients with infection using infection markers, particularly in infections associated with high mortality (pneumonia, bacteremia)[1,2,6-8,11,19-22]; *b)* establishing and evaluating recommendations to optimize the management of patients with severe sepsis or septic shock[3-5,16-18]; *c)* improving the use of antimicrobials to diminish the selection pressure on multidrug-resistant pathogens[13-15], and *d)* evaluating preventive measures to reduce the incidence of nosocomial infections caused by bacteria or fungi[9,10,12,23-27].

Identification of an infection in a critically ill patient implies the initiation of empirical therapy with 1 or more antibiotics. Diagnosis of infection is sometimes difficult, as the expression of the signs and symptoms of infection might not be clear enough or might be caused by a noninfectious process. However, when a severe infection does exist, early administration of empirical therapy and appropriateness of the antimicrobials selected are related to improved survival. The availability of infection markers that are sensitive and specific enough would aid decision-making–particularly in the more complex cases in which diagnosis is uncertain–and could help to avoid unnecessary delays in the prescription of antimicrobial therapy. Studies using markers such as procalcitonin and C reactive protein are an important starting point that might be useful not only for the initiation of empirical therapy, but also for the evaluation of the response and for deciding when to stop or change antimicrobial therapy[19-22]. However, more studies are needed to find a suitable place for such markers in daily clinical practice and to demonstrate that their use on a routine basis is really of benefit to infected patients. In other scenarios, such as invasive fungal infections (candidemia, systemic candidosis), in which such markers do not help decision-making, risk indexes such as the *Candida* score have been developed. This index, based on clinical and microbiological data, establishes the risk of fungal infection for individual patients and proposes that antifungal therapy be initiated as pre-emptive therapy in the highest-risk groups, even before the fungal infection has been proven[12]. This score should be validated prospectively, and its real clinical usefulness has yet to be demonstrated.

The development of guidelines for the treatment of infections represents an important improvement in the management of critically ill patients. The adaptation of the guidelines to local epidemiology (center and unit) further increases the probability that patients will receive appropriate therapy. The impact of adherence to these guidelines has recently been proved in patients with ventilator-associated pneumonia and community-acquired pneumonia[3,4]. However, the management of infection in the presence of severe sepsis or septic shock involves measures that go beyond the scope of antimicrobial therapy. A set of therapeutical measures has recently been proposed for these patients. Some should be administered during the first 6 hours, and the rest during the first 24 hours after diagnosis of the infectious process. These recommendations are original in that they are accompanied by a campaign–the Surviving Sepsis Campaign–aimed at the diffusion and implementation of the measures in hospitals, with the objective of reaching a 25% reduction in the mortality of severely infected patients. Some studies performed to evaluate the application of the campaign are now being published, and relevant benefits in terms of mortality, hospital and ICU stay, and costs are being observed[16,18]. In parallel, severity indexes that allow stratification of the risk of death based on clinical data on admission are being developed for some syndromes, such as community-acquired pneumonia[1]. These indexes help to select which patients would benefit from a more aggressive approach from the onset of infection.

The main risk for antimicrobial use in critically ill patients is multidrug resistance. The risk for the development of resistance in certain bacteria increases when the same antimicrobial or family of antimicrobials is used for long periods of time and when dosing is suboptimal (subinhibitory concentrations at the focus of infection). Duration of antimicrobial therapy is not well established for most types of severe infection. Thus, antimicrobials are often administered for 2 or 3 weeks, particularly in the case of bacteremia, abscesses, empyema, etc. The use of sympathicomimetic drugs (dopamine, noradrenaline) and diuretics increases the clearance of antibiotics, while many other circumstances increase the distribution volume for most drugs. In both cases, there is a high probability that the concentration of antimicrobials at the focus of infection is suboptimal if antimicrobials are administered at current recommended doses. Recognition of the need to use pharmacokinetic and pharmacodynamic parameters to adjust dosing in the most severely ill patients is one of the most significant recent improvements in the management of infection. Regrettably, the possibility of using plasma concentrations is limited to aminoglycosides and vancomycin in the case of antimicrobials, while blood level motoring is used only used in research protocols for the other most common antimicrobials but not as a clinical tool. In order to minimize the risk of resistance associated with overuse of a specific family of antimicrobials, cycling strategies have been proposed. Even though the rationale for such an approach is reasonable, the studies performed to evaluate their efficacy are confusing and not very reassuring. Antibiotic cycling has been proposed in different ways (successive restriction of a certain family over a period of several months, preferred use of a specific antimicrobial for different periods, consecutive changes of antimicrobials) with diverse levels of adherence[13-15]. Criteria used to evaluate the intervention have not been homogeneous, and, when the rate of multidrug-resistant pathogen has been used as an outcome measure, the results indicate that the strategy does not control the imported resistant pathogens (not covered by the antibiotic policy in the ICU) or the cross-transmission of these pathogens, which are frequent in ICUs. At present, this strategy cannot be recommended in routine clinical practice and should be limited to well-designed research protocols that evaluate its potential.

Between 10 and 15% of critically ill patients may develop a new infection during their hospital stay. Ventilator-associated pneumonia and primary catheter-related bloodstream infections are the most frequent. The fact that these infections are associated with high morbidity and mortality explains why different preventive strategies to reduce their frequency are being investigated. Oropharyngeal decontamination with antiseptic solutions (chlorhexidine) and the use of topical nonabsorbable antimicro-