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SPECIAL ARTICLE

The management of pneumonia in internal medicine

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KEYWORDS

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Abstract Pneumonia generates a high workload for internal medicine departments. Management of this disease is challenging, because patients are usually elderly and have multiple comorbid conditions. Furthermore, the interpretation and adherence to guidelines are far from clear in this setting. We report the opinion of 43 internists especially interested in infectious diseases that were questioned at the 2011 XXXII National Conference of Spanish Society of Internal Medicine about the main issues involved in the management of pneumonia in the internal medicine departments, namely, classification, admission criteria, microbiological workup, therapeutic management, discharge policy, and prevention of future episodes. Participants were asked to choose between 2 options for each statement by 4 investigators. Consensus could not be reached in many cases. The most controversial issues concerned recognition and management of healthcare-associated pneumonia (HCAP). Most participants were aware of the differences in terms of underlying diseases, etiological distribution, and outcome of HCAP compared with community-acquired pneumonia, but only a minority agreed to manage HCAP as hospital-acquired pneumonia, as suggested by some guidelines. A clinical patient-to-patient approach proved to be the option preferred by internists in the management of HCAP.

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PALABRAS CLAVE

Neumonía adquirida en la comunidad;

Tratamiento de la neumonía en medicina interna

Resumen La neumonía acarrea una importante carga de trabajo en los servicios de medicina interna. Puesto que los pacientes suelen ser de edad avanzada y presentan múltiples enfermedades comórbidas, su tratamiento es difícil. Además, en este contexto, la interpretación

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Neumonía asociada a la asistencia sanitaria;
Paciente hospitalizado con neumonía;
Medicina interna

de las guías publicadas, al igual que la adhesión a ellas, está lejos de ser clara. Describimos la opinión de 43 especialistas en medicina interna, especialmente interesados en las enfermedades infecciosas, que asistieron a la XXXII Conferencia Nacional de la Sociedad Española de Medicina Interna, celebrada en 2011, y a los que se formularon preguntas sobre los principales problemas relacionados con el manejo de la neumonía en los servicios de medicina interna, es decir, su clasificación, los criterios de ingreso, examen microbiológico, manejo terapéutico, normas de alta y prevención de futuros episodios. Para cada enunciado, redactado por 4 investigadores, los participantes tenían que elegir entre 2 opciones. En muchos casos no se alcanzó un consenso. Los problemas más controvertidos se relacionaron con el reconocimiento y el manejo de la neumonía asociada a la asistencia sanitaria (NAAS). La mayoría de los participantes conocían las diferencias con respecto a las enfermedades subyacentes, la distribución etiológica y el desenlace de la NAAS, comparado con la neumonía adquirida en la comunidad, pero solo una minoría estuvo de acuerdo en tratar la NAAS como una neumonía hospitalaria, según lo sugerido por algunas guías. En el manejo de la NAAS la opción preferida por los expertos en medicina interna fue establecer una estrategia clínica paciente a paciente.

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Introduction

Pneumonia is a frequent infection and a common cause of death. Hospitalization for pneumonia has been increasing in recent years.¹ Between 24% and 75% of patients hospitalized for pneumonia are cared for in internal medicine departments (IMDs).^{2–14} Various studies have shown that the morbidity of pneumonia is higher among patients attended in the IMDs than among those attended in other departments.^{6–9} However, only a few studies specifically analyze patients cared for in IMDs.

In recent years, *Infectious Diseases Society of America* (IDSA) and *American Thoracic Society* (ATS) have proposed classifying pneumonia acquired outside the hospital in two major groups: classic community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP).¹⁵ Acceptance of this classification and its significance is not universal.^{16,17} In fact, HCAP has not been considered as a distinct epidemiological group by *European Respiratory Society* and *European Clinical Microbiology and Infectious Diseases Society* in their recent document on the management of adult patients with lower respiratory tract infections.¹⁸ Multiple guidelines address the different issues of management of pneumonia.^{15,19,20} However, interpretation of and adherence to the guidelines in IMDs are far from clear.^{2–14} We recently evaluated some of the issues involved in CAP and HCAP in a nationwide study of pneumonia in IMDs in Spain (ENEMI study).²¹

The present paper assessed the opinion of internists interested in the management of infectious diseases on several issues related to the management of pneumonia in IMDs.

Methods

The principal investigator drafted a list of ten questions about controversial issues in the management of pneumonia in IMDs and committed four infectious diseases specialists to resume literature data on each item and to prepare two alternative answers for each question.

For the literature review, a PUB MED research with the key words "pneumonia" and "internal medicine" and the limits "English, Italian and Spanish languages" was done.

Since the purpose of our initiative was to point out specific aspects of the pneumonia management in IMDs and generate opinions about them, we did not believe it was necessary to standardize the literature review and response generation processes as indicated for studies aimed to assess the appropriateness of medical or surgical procedures.

All the material obtained was edited in a document that was sent to all the members of the ENEMI study group before the meeting. At the 2011 XXXII Congress of the Spanish Society of Internal Medicine (SEMI) there was a panel of 43 internists belonging to the Study Group for Infectious Diseases of the Spanish Society of Internal Medicine who chose one of the alternative answers for each question.

Results

All panel members answered all following questions (all questions and answers are summarized in appendix Table 1 in the supplementary material that accompanies the article).

Recognition of HCAP as a separate entity

Question 1: In your opinion, do microorganisms that are different from those that cause CAP cause HCAP?

Background. In their work on healthcare-associated bloodstream infections (BSIs), Friedman et al.²⁸ first showed that the etiology of these episodes was more similar to that of nosocomial BSIs than to that of community-acquired BSIs. The authors concluded recommending broad-spectrum empirical antibiotic therapy in patients with BSIs who had had previous contact with the healthcare system. The etiology of HCAP varies, while some centers detect pathogens similar to those found in patients with CAP,^{22–24} others report microorganisms similar to those found in patients with hospital-acquired pneumonia^{25–28} (appendix Table 2). In previous studies, the prevalence of multidrug-resistant microorganisms varied with the study population and was lower when no immunosuppressed patients who attended emergency departments were included^{22–24} and higher if hospitalized patients with any underlying conditions were included.^{25–28} To date, the ENEMI study is the only one to provide data on the etiology of HCAP among patients

hospitalized in IMDs, showing that, although *Streptococcus pneumoniae* was the main causative agent of HCAP episodes (38.5%), a high proportion of *Pseudomonas aeruginosa* (*P. aeruginosa*) (16.9%), methicillin-resistant *Staphylococcus aureus* (MRSA) (12.3%), and *Enterobacteriaceae* (12.3%) were found in that population. Furthermore, HCAP was one of the independent risk factors for difficult-to-treat (DTT) microorganisms (*P. aeruginosa*, MRSA, and *Enterobacteriaceae*) in patients with pneumonia cared for by IMDs.²¹

Responses. Panelists were invited to choose between the following two statements: (a) A high number (up to 30%) of cases of HCAP cared for in IMDs are caused by DTT microorganisms or (b) The etiology of HCAP is similar to that of CAP. Most panelists (92.9%) agreed that DTT microorganisms cause a significant rate of patients with HCAP hospitalized in the IMD. Therefore, most participants felt that it was important to recognize HCAP, since its therapy differs from that of CAP.

Question 2: Are the Pneumonia Severity Index (PSI) and CURB-65 scores useful when deciding the site of care of patients with CAP in IMDs?

Background. To reduce the rate of unnecessary hospitalizations, the guidelines of the IDSA for management of CAP recommend using the PSI or the CURB-65 scores when selecting the site of care (appendix Tables 3 and 4).¹⁹ However, in clinical practice, many patients with low-risk pneumonia are hospitalized, mainly in IMDs.^{2,3,6,12-14,29} Main reasons for these inappropriate hospitalizations are found in the concomitance of other medical conditions, social needs, oral intolerance, failure of outpatient therapy, noncompliance with therapy, hypoxemia, or suspicion of sepsis.^{14,30-34} In a study carried out in two Spanish hospitals, patients attended in the emergency department with low-risk CAP (PSI class II or III) were randomized to receive inpatient treatment with intravenous levofloxacin or to be discharged with oral levofloxacin. Immunocompromised patients and those with exacerbation of underlying diseases, respiratory failure, or social problems were excluded. The rate of cure was more than 80% for both groups, with a greater satisfaction among the outpatient group.³⁵ The authors conclude that in selected patients with low-risk CAP, according to the PSI, outpatient care provides greater patient satisfaction and is as safe and effective as hospitalization.

Responses. Panelists were invited to choose between the following two statements: (a) risk stratification scores are applicable in IMDs and are useful when selecting the site of care of CAP patients or (b) the decision on the site of care of CAP patients should be based only on clinical judgment. Overall, 88.1% of the panelists indicated that the pneumonia risk stratification PSI and CURB-65 scores are applicable in the IMDs and can guide decisions on the site of care of CAP patients. Only 11.9% of the members felt that decision on the site of care should be based on clinical judgment alone.

Question 3: Are the PSI and CURB-65 scores useful when selecting the site of care for patients with HCAP?

Background. Site of care for patients with HCAP is an unresolved issue. Some experts consider hospitalization necessary for all patients classified as having HCAP, because of the different etiologies, therapy requirements, and

prognosis of this population.³⁶ The value of the CAP scores to assess the site of care in HCAP patients is far from clear. Only one study has investigated the performance of different CAP scores to predict adverse outcome in patients with HCAP: PSI (>90) had the highest sensitivity in predicting mortality, followed by CURB-65 (≥ 2).³⁷ In an opinion document on HCAP published by Kollef et al., some experts proposed outpatient care for patients with low-risk pneumonia according to the PSI and/or CURB-65 scores, with a strict re-evaluation of patients at 48–72 h.³⁶ In the ENEMI study, 8% and 16% of HCAP patients had low-risk pneumonia according to the PSI (class II or III) and CURB-65 score (<2). Among these patients, the rate of in-hospital mortality was 3.8% and 2%, respectively. **Responses.** Panelists were invited to choose between the following statements: (a) PSI and CURB-65 scores are useful when deciding site of care for patients with HCAP or (b) All patients with HCAP should be hospitalized. Only 30% of the panelists considered the PSI and CURB-65 scores useful when deciding site of care for patients with HCAP, 16% considered necessary to hospitalize all patients with HCAP, and the remaining 54% thought that admission should be decided clinically on an individual basis.

Microbiological work-up and etiologic assessment

Question 4: In which patients with CAP or HCAP is it necessary to perform an etiological diagnosis, and which tests should be carried out?

Background. The indications for microbiological diagnostic tests in the diagnosis of CAP and HCAP are imprecise in most guidelines.^{15,19,20} The low yield of the microbiological workup and the favorable outcome usually obtained with empirical therapy have produced a decrease in the use of microbiological resources for the management of CAP patients.¹⁹ However, microbiological workup has been associated with a better outcome among patients hospitalized with pneumonia.^{21,38} The need for diagnostic testing is clear for patients with HCAP, in whom DTT microorganisms are more prevalent and empiric therapy can be inappropriate. International guidelines recommend performing blood cultures (BCs), Gram stain, sputum culture, and determination of urinary antigens for *Legionella pneumophila* serogroup 1 and *S. pneumoniae*.¹⁹ The main debate has centered around the need to perform BCs in all hospitalized patients with pneumonia because of their low yield and the possibility of false-positive results.³⁹ Patients with severe pneumonia or those with high serum levels of inflammatory markers such as procalcitonin, have been proposed as candidates for BC by some authors.⁴⁰ However, recognition of bacteremia is extremely important for adequate management of pneumonia in terms of additional investigations and duration of antibiotic therapy. In the ENEMI study, the overall yield of BCs was 8%; however, in patients with an etiological diagnosis, 18% of etiologies were determined by BCs.

Responses. Panelists were invited to choose between the following statements: (a) diagnostic testing to establish an etiological diagnosis should be carried out in all patients hospitalized with pneumonia or (b) diagnostic testing to establish an etiological diagnosis should be carried out only in selected groups of patients. Overall, 76.7% of the panelists favored a microbiological workup in all patients

hospitalized with pneumonia. Panelists were then asked if diagnostic testing should always include BCs or if BCs should be obtained only from selected patients. In the opinion of 88.4% of the panelists, diagnostic testing should always include BCs and determination of urinary antigens for *Legionella pneumophila* serogroup 1 and for *S. pneumoniae*. In addition, when available, a sputum culture should be processed using Gram stain.

Therapeutic management

Question 5: When is the best time to start antibiotic therapy in patients hospitalized with pneumonia?

Background. Early administration of antibiotic therapy has been considered a standard of care in the management of pneumonia since two retrospective studies showed that receiving the first antibiotic dose within 4–8 h of admission improved survival.^{41,42} Unfortunately, this figure was not confirmed by further prospective studies or meta-analyses.^{43,44} Furthermore, early administration of antibiotics has been criticized by some authors because of the potential for misdiagnosis of pneumonia, the risk of overuse of antibiotics, and the possibility of a lower yield in the microbiological workup.^{45,46} Thus, more recent guidelines do not specify a time window for delivery of the first antibiotic dose and merely suggest that it should be given in the emergency department.¹⁹ In most studies, early administration of therapy was associated with the severity of pneumonia (higher PSI score, altered mental status, multilobar pneumonia, need for admission to the intensive care unit [ICU])^{47,48}; consequently, the impact on mortality in these patients could be minimal because of the intensity of the inflammatory response. Other authors have shown a favorable impact of early antibiotic administration on the length of stay.^{49,50} We confirmed this finding in the ENEMI study, where 70% of the patients received the first dose of antibiotics within 6 h of the diagnosis of pneumonia. Early administration of therapy was not associated with lower mortality rate, independently of the PSI score and the adequacy of therapy, but was associated with fewer days of fever and more rapid clinical stability.

Responses. Panelists were invited to choose between the following two statements: (a) the first antibiotic dose should be administered within 6 h from the diagnosis of pneumonia or (b) the start of treatment should not interfere with diagnostic testing; therefore, it can be delayed for more than 6 h. All panelists agreed that the first antibiotic dose should be administered within 6 h of the diagnosis of pneumonia.

Question 6: How should patients with HCAP be treated empirically?

Background. The prevalence of DTT microorganisms in patients with HCAP varies according to the population included and the study site. Thus empirical therapy of HCAP remains controversial.¹⁷ In fact, despite the recommendation of the ATS to treat these patients in the same way as those with hospital-acquired pneumonia,¹⁵ adherence to these guidelines is poor in clinical practice.⁵¹ Some authors have suggested that patients with HCAP comprise a heterogeneous population in which not everyone has the same risk for DTT microorganisms.^{16,52} Consequently,

studies have been performed to identify factors associated with DTT microorganisms among HCAP patients. Shorr et al. first showed that the broad definition of HCAP had a specificity of only 48.6% for resistant infections.⁵² The variables found to be independently associated with resistant pathogens (*P. aeruginosa* and MRSA) were recent hospitalization, residence in a nursing home, hemodialysis, and admission to the intensive care unit. The authors proposed a scoring system, assigning 1, 2, 3 or 4 points for each variable, respectively. Among patients with fewer than 3 points, the prevalence of resistant pathogens was less than 20%, compared with 55% and more than 75% in persons with scores ranging from 3 to 5 and more than 5 points, respectively. This score has been further validated, showing a high negative predictive value (84.5% for score=0) and leading to fewer patients being unnecessarily treated with broad-spectrum antibiotics.⁵³ Hospitalization in the preceding 90 days and residence in a nursing home were the independent risk factors for multidrug-resistant pathogens in another study of hospitalized patients with community-onset pneumonia.⁵⁴ In the ENEMI study, the only variable independently associated with DTT microorganisms among patients with HCAP was regularly attending a hospital for treatment of a chronic disease (OR, 4.12; 95% interval confidence, 1.43–11.84; $p=0.008$). Further studies of the factors associated with DTT microorganisms among patients with pneumonia hospitalized in IMDs are necessary to design the best approach in this setting.

Responses. Panelists were invited to choose between the following statements: (1) All patients who fulfilled HCAP criteria should be treated empirically with broad-spectrum antibiotic therapy or (2) The empirical antibiotic therapy of patients classified as having HCAP should be tailored to the underlying conditions and severity of pneumonia. Overall, 93% of the panelists agreed that empirical therapy of HCAP should be individualized.

Question 7: Is it necessary to know the etiology before de-escalating antimicrobial therapy in patients with HCAP?

Background. De-escalation is safe and useful in the treatment of ventilator-associated pneumonia (VAP) to reduce antibiotic pressure and risk of toxicity. It has been recommended in the management of patients with HCAP.¹⁵ However, in this setting, the yield of diagnostic testing is lower than in patients with VAP, so few patients may be candidates for de-escalation. It has been proposed that de-escalation should be performed in patients with culture-negative results and prompt good clinical response,³⁶ since there is evidence that these patients have milder disease and better outcome than HCAP patients with culture-positive samples.⁵⁵ To date, the only study to analyze the safety of de-escalation to a fluoroquinolone in patients with HCAP and negative cultures revealed a shorter hospital stay, lower hospital costs, and lower mortality rates.⁵⁶

Responses. Panelists chose between the following statements: (a) de-escalation may be applied only in HCAP patients with known etiology or (b) de-escalation may be applied in patients with HCAP and in patients with negative results of microbiological techniques but a good clinical response. Overall, 83.7% agreed that de-escalation could

be applied in patients with negative cultures, while 16.3% deemed de-escalation applicable only to patients with a known etiology.

Question 8: How long should patients with CAP and HCAP be treated?

Background. The recommended duration of antimicrobial therapy for CAP patients is 7–10 days. In recent years, randomized clinical trials have shown that the cure rate is similar for patients with mild-moderate CAP – whether hospitalized or not – treated for 3–7 days and for those treated for more than 7 days, independently of the antimicrobial drug administered.^{57,58} The latest IDSA/ATS guidelines on the management of CAP recommend treating patients for up to 5 days and then stopping therapy if they are afebrile and clinically stable from 48 to 72 h.¹⁹ In patients with extra-pulmonary complications such as bacteremia or meningitis, those with an etiological diagnosis who have received inappropriate initial therapy, and those with isolation of difficult-to-eradicate microorganisms such as *P. aeruginosa*, a more prolonged antimicrobial course is recommended. As for the duration of antibiotic therapy, no studies have investigated the safety of a short course of therapy in patients with HCAP. Current recommendations are the same as for hospital-acquired pneumonia: one week for patients with no extra-pulmonary complications and isolation of easy-to-treat pathogens and two weeks for pneumonia caused by *P. aeruginosa* and MRSA.¹⁵ Physicians should be aware of risk factors for persistent or recurrent infection, such as bronchiectasis, bronchial stenosis, and cavities, and in these patients prolonged therapy should be considered.

Responses. Panelists were invited to choose between the following: (a) The antimicrobial course for CAP should not be longer than 7 days or (b) The antimicrobial course for CAP should not be shorter than 10 days. Most panelists (93%) agreed that the antimicrobial course for CAP should not be longer than 7 days. As for HCAP, panelists were invited to one of the following options: (a) the length of antimicrobial course for HCAP should be similar to that of hospital-acquired pneumonia or (b) the length of antimicrobial course for HCAP should be similar to that of CAP. Most panelists (93%) agreed that the antimicrobial course for HCAP should be similar to that of hospital-acquired pneumonia.

Discharge policy and prevention of future episodes

Question 9: When should a patient with pneumonia be discharged?

Background. Current IDSA/ATS guidelines on the management of CAP recommend switching to oral therapy and discharging patients as soon as they are clinically stable and tolerate oral administration (appendix Table 5).¹⁹ In the ENEMI study, only 60% of the patients switched to oral therapy. In addition, patients remained hospitalized a median of 4.9 days after being achieved clinical stability. In a survey, physicians stated that the main reasons for delayed discharge of patients treated for pneumonia were management of medical conditions other than pneumonia (56%), end of the standard course of therapy (15%), and organization of outpatient care (14%).⁵⁹ In the case of underlying diseases,

there is frequently no opportunity for interventions. However, the other reasons are open to improvement. Clinical observation after achievement of clinical stability and in-hospital completion of antibiotic therapy have been shown to be unnecessary and potentially dangerous for patients.¹⁹ Furthermore, Carratala et al. showed recently that a 3-step pathway including early mobilization, use of objective criteria for switching to oral antibiotic therapy, and for deciding on hospital discharge was safe and effective in reducing the duration of intravenous antibiotic therapy and the length of stay in patients hospitalized with CAP.⁶⁰

Responses. Panelists were invited to choose between the following statements: (a) Patients may be discharged as soon as they become clinically stable and tolerate oral therapy or (b) Patients should remain under observation in hospital 24–48 h after becoming clinically stable. Overall, 76.7% of the panelists agreed that patients could be switched to oral therapy and discharged as soon as they are clinically stable and tolerate oral administration, while 23.3% considered that patients should remain under observation for 24–48 h after becoming clinically stable.

Question 10: What is the best strategy in IMDs for preventing future episodes of pneumonia?

Background. Vaccination against influenza and *S. pneumoniae* is a cost-effective measure for preventing pneumonia and is considered standard of care in managing CAP patients.⁶¹ However, the rate of vaccination (influenza and pneumococcal polysaccharide) for individuals ≥ 65 years or with comorbid conditions ranges from 37% to 69%.^{62,63} To enhance these rates, all patient contacts with the healthcare system should be viewed as opportunities for vaccination. However, the rate of in-hospital vaccination is very low, ranging from 2% to 7%.^{21,63} Multidisciplinary interventions have been proposed to improve this percentage, including electronic screening to identify eligible unvaccinated patients.⁶⁴ Current guidelines on the management of CAP recommend investigating the vaccination status of patients admitted with pneumonia and, if indicated, vaccinating patients at discharge after resolution of fever.¹⁹

Responses. Panelists were invited to choose one of the following statements: (a) screening of vaccination status and, if indicated, recommendations about vaccination should be included in the discharge report or (b) prevention of future episodes should be managed exclusively by family physicians. Overall, 83.7% of the panelists agreed that vaccination status should be investigated in all patients admitted for pneumonia to the IMD and, if indicated, vaccination should be recommended in the discharge report, while 16.3% of panelists stated that the prevention of future episodes should be the responsibility of family physicians.

Conclusions

Our manuscript presents a literature review and the opinion of internists on several issues in the management of pneumonia in IMDs. Regarding the significance of HCAP, most internists of our panel were aware of the differences between CAP and HCAP in terms of etiological distribution and outcome, but only a minority favored management of HCAP as hospital-acquired pneumonia, as suggested in

some guidelines. A clinical patient-to patient approach was the preferred attitude for management of HCAP. Furthermore, we pointed out some concerned and unresolved issues such as the use of microbiology, timing of administration of the first antibiotic doses, the use of de-escalation therapy in HCAP patients, and strategy for prevention of future episodes. Most internists agreed about the need to attempt an etiological diagnosis in all the patients with pneumonia hospitalized in IMDs. They also stated that diagnostic testing should include always blood cultures unlike international guidelines do not recommend so. Although the early (within 6 h of pneumonia diagnosis) administration of empirical antimicrobial therapy is no longer considered a standard of care, all the internists favored this recommendation. Regarding the use of de-escalation therapy in HCAP, almost 84% of internists stated that it might be applied in the patients with good clinical response to the empirical broad-spectrum therapy even if the microbiological results are negative. Finally, as for prevention of future episodes, the majority of internists stated that patients admitted for pneumonia should be screened for the vaccination status and, if indicated, recommendations about vaccination should be included in the discharge report.

Further studies are needed to address the impact of these recommendations on the clinical outcome of patients with pneumonia cared for by IMDs.

Conflicts of interest

This study does not present any conflict of interest for the authors.

Transparency declaration

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.rce.2013.03.001>.

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