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REVIEW

Management of Health-Care Associated Pneumonia (HCAP)

Gestione della Polmonite associata all'Assistenza (HCAP)

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KEYWORDS

Health Care Associated Pneumonia (HCAP); Community Acquired Pneumonia (CAP); Hospital Acquired Pneumonia (HAP); Multidrug-resistant (MDR) Pathogens.

Summary

Introduction: The traditional classification of Pneumonia as either community acquired (CAP) or hospital acquired (HAP) reflects deep differences in the etiology, pathogenesis, approach and prognosis between the two entities. Health-Care Associated Pneumonia (HCAP) develops in a heterogeneous group of patients receiving invasive medical care or surgical procedures in an outpatient setting. For epidemiology and outcomes, HCAP closely resembles HAP and possibly requires an analogous therapeutic regimen effective against multidrug-resistant pathogens.

Materials and methods: We reviewed the pertinent literature and the guidelines for the diagnosis and management of HCAP to analyze the evidence for the recommended approach.

Results: Growing evidence seems to confirm the differences in epidemiology and outcome between HCAP and CAP but fails to confirm any real advantage in pursuing an aggressive treatment for all HCAP and CAP patients.

Discussion: Further investigations are needed to establish the optimal treatment approach according to the different categories of patients and the different illness severities.

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Community-acquired Pneumonia (CAP) and hospital-acquired Pneumonia (HAP) are different in their etiology, pathogenesis, diagnostic and therapeutic approach and prognosis (Table 1).

According to current guidelines, most patients with CAP should be treated empirically as outpatients with oral antibiotics and microbiological investigations are not recommended [1,2]. Illness severity is the main prognostic factor, and

the decision to hospitalize is based on the clinical evaluation, preferably validated by at least one objective tool of risk assessment, such as the Pneumonia Severity Index (PSI) or the CURB index [3–5]. The main prognostic factor for patients with HAP is inappropriate initial antimicrobial treatment. The delays in the administration of appropriate therapy have been associated with excessive hospital mortality and

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Table 1 CAP and HAP: comparison of clinical characteristics and suggested management.

	CAP	HAP
Etiology	Pneumococcus, Mycoplasma, Haemophilus, Legionella	Enterobacteriaceae, Pseudomonas, Staphylococcus aureus
Pathogenesis	Inhalation	Oropharyngeal colonization
Microbiological investigation	Only in severe illness (hospitalized)	Ever
Therapeutic approach	Empiric	Empiric → Specific
Negative prognostic factor	Illness severity	Delayed effective therapy
Prognosis	Mostly good	Mostly severe

changing antimicrobial therapy once culture results are available may not reduce the risk [6,7]. As a consequence, the HAP patient treatment approach requires the collection of respiratory secretions and blood for cultures, promptly followed by a broad-spectrum empiric antibiotic therapy that, for HAP occurring more than 4 days after hospitalization (late-onset HAP) and in patients with risk factors for multi-drug-resistant (MDR) pathogens, should be effective against methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas* species. To avoid the overuse of broad-spectrum antibiotics, initial therapy should be de-escalated on the basis of microbiological results [8,9].

In the last decade, however, an increasing number of patients receive invasive medical therapy or surgical procedures in outpatient settings (nursing homes, rehabilitation hospitals and day surgery facilities) or the patients frequently return to the hospital a short time after discharge. A large body of evidence suggests that the infections occurring in these HCAP patients closely resemble hospital-acquired infections with respect to their epidemiology and outcomes and possibly require an analogous management approach. Among health-care associated infections, health-care associated pneumonia (HCAP) has been extensively investigated.

Between January 1, 2002 and December 31, 2003, Kollef et al. retrospectively analyzed a large multi-institutional database collecting the microbiological and clinical data of 3209 patients admitted to 59 US acute-care hospitals with microbiologically documented pneumonia [10]. Out of these, 69.3% had true CAP and 30.7% had been categorized with HCAP based on the following patient characteristics: they were transferred from another health-care facility, they were on long-term hemodialysis or they had been hospitalized within the preceeding 30 days. HCAP cases were comparable to HAP cases in etiology, *S. aureus* and *Pseudomonas* species were major pathogens in both groups, and prognosis, the mortality rate was 19.8% in the HCAP group and 18.8% in the HAP group. The authors suggested distinguishing the HCAP from the CAP cases when selecting an empirically-driven antibiotic treatment. In other reports, the incidence of HCAP among patients admitted to the hospital with pneumonia ranged between 19% and 52% [11,12]. Micek et al. prospectively confirmed that most patients (67.4%) with documented microbiological pneumonia that required hospitalization, and who were traditionally categorized as CAP, were actually HCAP. In this setting, the incidence of MDR bacteria (MRSA, 24.6%; and *Pseudomonas* species, 18.8%) and the mortality rate (24.6%) were significantly greater than

among patients with CAP [13]. In Italy, nursing home residents with pneumonia that was treated as CAP had a 24% mortality rate, compared with a 9.8% mortality rate among true CAP patients [14].

Since 2005, international guidelines have recommended the inclusion of HCAP in the spectrum of HAP and VAP (ventilator-associated pneumonia). These guidelines are: to hospitalize the HCAP patients, to treat them empirically with broad-spectrum antibiotics active for MDR pathogens and to de-escalate the antibiotics on the basis of clinical and microbiologic data to limit the emergence of drug resistance in the hospital [15].

The recommended approach, however, is problematic:

- 1) The recommendation is that all health-care patients should be hospitalized and treated for MDR microorganisms, a unilateral decision made independently from clinical status and severity score. Particularly troublesome is that all residents in nursing home diagnosed with HCAP are to be moved into an acute-care hospital, despite the growing evidence that hospitalization does not reduce mortality from HCAP. Moreover, hospitalization increases cost to the patient and increases the risk for functional decline, delirium and pressure ulcers [16,17].
- 2) The recommendation indicates that all emergency departments should adequately collect the respiratory secretions (endotracheal aspirate, bronchoalveolar lavage or protected brush specimen) within 1-2 hours, before initiating empiric antibiotic treatment. The main risk of waiting on microbiological investigations is the delay in starting the antibiotic treatment. The major advantage is to allow for the de-escalation from broad-spectrum drugs to a pathogen specific therapy.
- 3) The recommendation proposes that empiric treatment should be broad-spectrum and target MRSA and *Pseudomonas*. As a consequence, vancomycin, linezolid, carbapenems or anti-pseudomonas beta-lactams should be used. However, the incidence of MDR bacteria in HCAP widely ranges in different institutions. Among 126 HCAP cases studied in Spain, *Staphylococcus aureus* and *Pseudomonas* were isolated in 2.4% and 1.6%, respectively [18]. Furthermore, only a minority of HCAP (32.5-49.5%) cases are microbiologically documented [18,19] and can have the initial empiric therapy de-escalated. In culture-negative HCAP, the initial empiric treatment should probably be continued for 10-14 days. The large empiric use of glycopeptides, linezolid and carbapenems could be associated to increased toxicity, prolonged hospital-stay,

Table 2 Controversial issue in management of HCAP.

	Aggressive approach	Prudent approach
Hospitalization	All patients	Only in severe illness
Microbiological investigation	Ever	Only in severe illness
Risk for MDR pathogens	High in all patients	Different for patient's category
Empiric therapy	Target to MDR pathogens	Broad spectrum
De-escalation therapy	If no MDR pathogens before antibiotic therapy	If no MDR pathogens during antibiotic therapy
Negative prognostic factor	Delayed effective therapy	Illness severity

relevant costs and an increased emergence rate of MDR bacteria.

- 4) The risk of infections due to MDR bacteria could vary for different categories of HCAP patients. To avoid an overuse of antibiotics, it has been proposed to calculate this variable risk using a score (assigning 4, 3, 2 and 1 points, respectively, for recent hospitalization, nursing home residence, hemodialysis and intensive care unit admission). Among patients with fewer than 3 points, the prevalence of resistant pathogens is <20%, compared with 55% and >75% if the score is from 3 to 5 or >5, respectively [20]. Clinical practice and recent literature have also suggested new risk factors for MDR pathogens such as the presence of permanent indwelling devices, antibiotics use within the preceding 3 months, chronic or advanced pulmonary diseases, history of alcoholism and immunosuppression [21]. A review of recent literature indicates that the major risk factors for MDR pathogens are severe illness, hospitalization in the past 90 days, antibiotic therapy in the past 6 months, poor functional status and immunosuppression [22].
- 5) The relationship between differing outcomes for HCAP compared with CAP, MDR etiology and inappropriate treatment remains controversial. In a recent series [23], among the patients with bacteremic pneumococcal pneumonia, 184 were classified with CAP and 44 as HCAP. Despite the fact that only three isolates (1.5%) were resistant to beta-lactams and only two patients received inappropriate therapy, mortality was significantly higher in the HCAP cohort than in the CAP cohort (29.5% versus 7.6%). These results were probably related to differing illness severities (PSI >90 in 95% of HCAP patients and in 65% of CAP patients). In another series, when compared with CAP patients, HCAP patients had a higher mortality rate (19.2% vs. 7.4%), a higher incidence of MDR pathogens (29.3% vs. 13.0%) and were more frequently inappropriately treated (24.6% vs. 8.7%) but also had a significantly higher PSI score [12]. Again, the advantages of treating HCAP as HAP are not well documented. Among 334 nursing home patients with pneumonia, results (in terms of time to clinical stability, in-hospital mortality and 30-day mortality) obtained among the patients treated as CAP cases (77%) and patients treated as HAP cases (23%) were comparable [24]. Furthermore, an online survey sent to 1313 physicians revealed that despite 71% of them reporting being aware of the current guidelines, and 79% agreeing with the guideline recommendations, 78% would treat HCAP as CAP [25].

- 6) The new approach to HCAP is based on data derived from a culture-positive HCAP series. Recently, Micek and Kollef compared the culture-negative (50.5%) cases with the culture-positive HCAP cases of their series. The culture-negative group included patients who had no respiratory cultures obtained (66.1%) and patients with cultures yielding no pathogens (33.9%). The patients in this group had a lower severity of illness, lower hospital mortality (7.4% vs. 24.6%) and shorter hospitalization (6.7 vs. 12.1 days), resembling CAP [19]. As a consequence, patients with culture-negative HCAP could be safely de-escalated to CAP therapy [26].

In conclusion, the management of HCAP remains controversial (Table 2). According to the present guidelines, all HCAP patients should be identified, hospitalized, sampled for cultures and treated with broad spectrum antibiotics active against *Pseudomonas* and MRSA. Initial treatment should be de-escalated according to microbiological results in culture-positive patients. Culture-negative patients with a favorable clinical evolution could probably be treated as CAP patients and eventually discharged. The recommendations indicate that facilities for adequate specimen collection and culturing should be available in the emergency department.

Moreover, these recommendations are based on data regarding HCAP patients addressed to the emergency department and hospitalized. More specific criteria for hospitalization are probably needed, based on the assessment of the relative weight of antibiotic resistance versus illness severity as a prognostic risk factor, particularly in the subset of nursing home-acquired pneumonia.

Further studies are needed to determine the optimal management of HCAP patients treated at home as CAP patients.

Conflict of interest

The authors have no conflict of interest to disclose.

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