

Antimicrobial Therapy for Patients with Community-Acquired Pneumonia in the Emergency Department: Results from a French National Audit

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Citation: Ducasse J, Pateron D, Vernet-Garnier V, Fontaine J, Pourcel L, et al. (2016) Antimicrobial therapy for patients with community-acquired pneumonia in the emergency department: results from a French national audit. Emerg Med Inves 2016: G112.

Received Date: 3 October, 2016; **Accepted Date:** 20 October, 2016; **Published Date:** 28 October, 2016

Declaration of interest: This study was supported by institutional grants provided by the French National Authority for Health "Haute Autorité de Santé" (HAS).

Abstract

Background: The updated French guidelines for the management of antimicrobial therapy and site-of-care for adults' community-acquired pneumonia (CAP) were published in July, 2010, stratifying patients in 6 groups depending on age, significant underlying disorders and organ failure.

Objectives: We conducted the first national audit of adherence to the latest CAP guidelines.

Methods: A web-based audit tool was developed as part of the guidelines. French Emergency Departments (EDs) were invited to participate in the audit capturing data on adults visiting EDs with suspected CAP within the study period (15th October-15th December, 2010).

Results: A total of 3,166 cases were provided from 72 EDs. Median age was 75 years (range 15-106 years), 55% were male. CRB65 score was 0 in 22.9%, 1-2 in 67.8%, and 3-4 in 9.2%; 2,630 (83.5%) patients were admitted after ED visit including 335 (12.7%) in intensive care units. Median delay to first antibiotics was 3h45 min. Initial empirical antimicrobial treatment was in accordance with French CAP guidelines in 895 (28.3%) patients. However, adherence widely varied (0%-66.9%) in the patient groups. Of note, 354 (11.2%) did not receive any antibiotics and antimicrobial agents were not in adherence with guidelines in 1,917 (60.5%) patients.

Conclusions: Management of CAP often differs from guidelines in French emergency departments. This result questions whether emergency physicians are aware of the recommendations or whether recommendations are adequate for emergency CAP patients.

Keywords: Audit; Antimicrobial agent; Emergency department; Community-Acquired pneumonia; Site of care

Introduction

Community-Acquired Pneumonia (CAP) is a potentially serious infectious disease that frequently occurs in Emergency Department (ED) patients. Based on initial assessment, physicians have to decide on antimicrobial therapy and in-hospital site-of-care. Providing adequate management to CAP patients impacts both outcome and related costs [1]. Guidelines are developed and widely broadcasted to help practitioners. Delay of antimicrobial agents is regarded as an indicator for quality of care in CAP patients as it has been associated with outcome [2]. Therefore, optimizing initial antimicrobial therapy is a major goal for the CAP guidelines. French Drugs Administration (Agence française de sécurité sanitaire des produits de santé, Afssaps) and National Society for Infectious Disease (Société de pathologie infectieuse de langue française, Spilf) released reference guidelines on 21st of July, 2010 [3]. These recommendations were supposed to update and improve administration of antibiotics in CAP patients. Unfortunately, making a diagnosis of CAP in emergency patients remains challenging as clinical signs are aspecific and X-ray results are often unsatisfactory [4]. This may lead to uncertain diagnosis and inadequate antimicrobial treatment [5,6].

Here we investigated whether the recent CAP guidelines for antimicrobial therapy in CAP were followed by emergency physicians at bedside and whether factors were associated to non-adherence to antibiotic guidelines.

Methods

The French National Authority for Health (Haute Autorité de Santé, HAS) released methodological guidelines for conducting an audit in the setting of healthcare. This methodology was used for the present study. We developed an electronic case report form on CAP management in the ED. An invitation to participate was electronically mailed to medical heads of 200 EDs, on behalf of the French College of Emergency Medicine (Collège Français de Médecine d'Urgence, CFMU) and the French Society of Emergency Medicine (Société Française de Médecine d'Urgence, SFMU). Centers that aimed to participate in the survey had to register before 15th of October, 2010. Users that registered were asked to capture data on patients visiting EDs with suspected CAP during the study period, 15th of October to 15th of December 2010. Patients aged > 15 years could be included if they visited the ED with a suspicion of CAP based on the attending physicians' evaluation whatever the results of clinical examination, laboratory data and chest X-rays. For this observational study, we did not exclude patients.

Study protocol and procedures complied with the principles of the Declaration of Helsinki. The institutional review board for the protection of human subjects approved the study protocol and

patient informed consent procedures.

We recorded characteristics of EDs: setting (general hospital, tertiary teaching hospital, private hospital); annual number of visits; number of beds available in the emergency observation unit; organization and management of antimicrobial agents in the ED (computerized prescription; ED procedures for prescription referring to guidelines; computerized microbiological results; regular feed-back about consumption; ED expert for the use of antimicrobial agents; ED audit for antimicrobial use for the preceding 2 years; information about adequate use of antimicrobial therapy delivered at the hospital level).

Data collected from patients included: demographics (age, gender); origin (home, nursing home, rehabilitation centre, other); previous medical history and underlying disorders (COPD, cystic fibrosis, cerebrovascular disease, congestive heart failure, immune suppression, active neoplasm, chronic renal failure, liver disease, sickle cell disease, admission for the preceding year, previous community-acquired pneumonia); social / organizational barriers (unfavorable social conditions, isolation, perceived risk for unsatisfactory treatment compliance); use of antimicrobial agents within 7 days prior to ED visit, and main clinical characteristics (pulse oximetry <90% in room air, respiratory rate, heart rate, systolic and diastolic arterial blood pressure, impaired consciousness or abnormal mental status). CRB65 was calculated for each patient: for this scoring system, one point is awarded for each of the following features: Confusion – recent; Respiratory rate 30 breaths/min or greater; Blood pressure-systolic of 90 mmHg or less or a diastolic of 60 mmHg or less; 65 years of age or older. Results of chest X-ray were recorded (local infiltrate, pleural effusion, collection). Antimicrobial therapy was registered as well as qualification of the prescriber (senior or junior physician). Delay of initial antimicrobial dose administration was calculated using date-stamps. Finally, we collected ED length of stay, death (if it occurred in the ED) and site-of-care after ED visit.

We compared adherence to guidelines according to pre-defined patients' categories, i.e. group 1: CAP patients < 65 years without signs and symptoms of severity, group 2: CAP patients < 65 years with significant underlying disorders and >65 years without signs and symptoms of severity, group 3: CAP patients < 65 years during seasonal flu without signs and symptoms of severity, group 4: CAP patients < 65 years with significant underlying disorder and > 65 years during seasonal flu without signs and symptoms of severity, group 5: CAP patients without COPD and cystic fibrosis, and group 6: CAP patients with COPD and cystic fibrosis and symptoms of severity. Table 1 summarizes guidelines for each of the above mentioned categories. Of note, guidelines determined signs and symptoms of severity as follow: respiratory rate >30 / min, heart rate > 120 / min, systolic arterial blood pressure < 90mmHg, impaired consciousness or abnormal mental status, association with active neoplasm.

| | Group 1 | Group 2 | | Group 3 | Group 4 | | Group 5 | Group 6 |
|------------------------|--|--|-------------|--|--|-------------|--|---|
| Age (yrs) | < 65 | <65 | >= 65 | < 65 | <65 | >= 65 | Indifferent | Indifferent |
| Underlying disorders | No | Yes | Indifferent | No | Yes | Indifferent | Indifferent | Indifferent |
| COPD & cystic fibrosis | No | No | No | No | No | No | No | Yes |
| Severity symptoms | No | No | No | No | No | No | Yes | Yes |
| Seasonal influenza | No | No | No | Yes | Yes | Yes | Indifferent | Indifferent |
| First line antibiotics | Amoxicillin or Pristiniamycin or Telithromycin or Macrolid | Amoxicillin-clavulanic acid or Levofloxacin or Cefotaxim or Ceftriaxon | | Amoxicillin-clavulanic acid or Pristiniamycin or Telithromycin | Amoxicillin-clavulanic acid or Levofloxacin or Cefotaxim or Ceftriaxon | | Cefotaxim or Ceftriaxon combined with Macrolid or Levofloxacin | Anti-Pseudomonas b-lactam combined with Aminoglycosid combined with Macrolids |

Table 1: Synoptic table of 2010 French recommendations for first line antimicrobial agents. Underlying disorders refer to at least one of the following condition: cerebrovascular disease, congestive heart failure, immune suppression, active neoplasm, chronic renal failure, liver disease, sickle cell disease; signs and symptoms of severity; COPD: chronic obstructive pulmonary disease.

Statistical analysis

Data entry using the web-based audit tool closed in January, 2011. The Chi-square or Fisher exact test (discrete variables) and the Student t-test (continuous variables) were used to compare the non-adherence to antibiotic guidelines. Univariate logistic regression analyses of factors previously reported to be associated was performed. Variables with $p < 0.25$ were entered into the multivariate stepwise backward model to identify predictors of non-adherence to antibiotic guidelines. Results from the logistic regression analyses are reported as odds ratios (OR) [95% confidence intervals (CI)] from the unadjusted and final models with p from the likelihood ratio test. All reported p values are two sided; p values < 0.05 were considered to be statistically significant for univariate analysis. All statistical analyses were done using SAS 9.4.

Results

Study population

Of the 82 EDs that initially registered, 72 answered the questionnaire and included patients (Table 2). Most EDs set in a primary care general hospitals in French metropolitan area, 3 centers were ultramarine and one set in the Principality of Monaco. Of the 3.166 CAP, 1690 (53%) were included in tertiary teaching hospitals. Characteristics of the study population are described in Table 3. Briefly, 55% were male, median age was 75 years, ranging from 15 to 106. A majority presented with significant underlying condi-

tions, mostly CHF and COPD. More than 10% had cerebrovascular disorders or active neoplasm. Among these, 22 (6%) suffered from chronic heart failure. Clinical signs of severity at presentation were frequent, as 526 (17%) patients had systolic blood pressure below 90mmHg and diastolic blood pressure below 60mmHg, 503 (16%) impaired neurological status, 714 (23%) respiratory rate above 30/min, and SpO₂ was below 90% in 1,954 (62%). We observed that 2.440 (77%) had CRB65 >1, 2.630 (84%) patients were hospitalized, 335 (11%) were admitted in ICU, and 36 (1%) died during their ED stay.

| | Total n (%) |
|--|----------------|
| Setting | |
| General and private hospitals | 41 (57) |
| Tertiary teaching hospitals | 31 (43) |
| > 45,000 annual number of ED visits | 19 (26) |
| > 15 beds in the ED observation unit | 22 (31) |
| ED and hospital management of antibiotics | |
| Computerized prescription | 43 (60) |
| ED procedures for prescription referring to guidelines | 39 (54) |
| Computerized microbiological results | 58 (81) |
| Regular feed-back about antibiotics consumption | 37 (51) |

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| | |
|---|---------|
| ED referent for the use of antimicrobial agents | 36 (50) |
| ED audit for antimicrobial use for the preceding 2 years | 23 (32) |
| Information about adequate use of antibiotics at the hospital level | 43 (60) |

Table 2: Characteristics of the 72 Emergency Departments that participated to the audit. Results are presented as number (percent%) as indicated. ED: Emergency Department

| | Total | | Adherence | | Non adherence | | P |
|--|--------------|------|--------------|------|---------------|------|--------------------|
| | (N = 3 166) | | (N = 895) | | (N = 1 917) | | |
| | n | % | n | % | n | % | |
| Demographic factor | | | | | | | |
| Male sex | 1 750 | 55.3 | 474 | 53.0 | 1093 | 57.0 | 0.0437 |
| Age (years) | 69.1 ± 19.6 | | 70.3 ± 19.7 | | 68.8 ± 19.6 | | 0.0493 |
| Age >= 65 years | 2033 | 64.2 | 617 | 68.9 | 1196 | 62.4 | 0.0007 |
| Nursing home resident | 440 | 13.9 | 102 | 11.4 | 296 | 15.5 | 0.0042 |
| Comorbid conditions | | | | | | | |
| COPD | 679 | 21.4 | 214 | 23.9 | 386 | 20.1 | 0.0228 |
| Cysticfibrosis | 8 | 0.3 | 1 | 0.1 | 3 | 0.2 | 10.000 |
| Liverdisease | 84 | 2.7 | 13 | 1.5 | 61 | 3.2 | 0.0076 |
| Congestive heartdisease | 824 | 26.0 | 258 | 28.8 | 488 | 25.5 | 0.0593 |
| Cerebrovasculardisease | 354 | 11.2 | 73 | 8.2 | 259 | 13.5 | < 0.0001 |
| Chronicrenaldisease | 275 | 8.7 | 68 | 7.6 | 176 | 9.2 | 0.1648 |
| Active neoplasm | 400 | 12.6 | 9 | 1.0 | 339 | 17.7 | < 0.0001 |
| Immune depression | 255 | 8.1 | 70 | 7.8 | 167 | 8.7 | 0.4286 |
| Sicklecelldisease | 8 | 0.3 | 2 | 0.2 | 6 | 0.3 | 10.000 |
| Previouscommunity-acquiredpneumonia | 477 | 15.1 | 15.1 | 132 | 14.7 | 288 | 15.0 |
| Social / organizationalconstraints | | | | | | | |
| Hospitalization for the previous year | 846 | 26.7 | 214 | 23.9 | 548 | 28.6 | 0.0094 |
| Unfavorable social conditions | 188 | 5.9 | 38 | 4.2 | 129 | 6.7 | 0.0094 |
| Isolation | 124 | 3.9 | 32 | 3.6 | 80 | 4.2 | 0.4502 |
| Unsatisfactorycompliance | 210 | 6.6 | 49 | 5.5 | 141 | 141 | 0.0642 |
| Antimicrobial agents within 7 days | 727 | 23.0 | 166 | 18.5 | 434 | 22.6 | 0.0136 |
| Clinicalcharacteristics | | | | | | | |
| Pulse oxymetry< 90% (room air) | 1954 | 61.7 | 652 | 72.9 | 1068 | 55.8 | < 0.0001 |
| Respiratory rate (cycles/min) | 23.8 ± 7.7 | | 21.2 ± 5.7 | | 25.1 ± 8.2 | | < 0.0001 |
| >= 30 cycles / min | 714 | 22.6 | 85 | 9.5 | 562 | 29.3 | < 0.0001 |
| Heart rate (bpm) | 96.8 ± 21.1 | | 90.2 ± 16.4 | | 100.0 ± 22.4 | | < 0.0001 |
| Systolic arterial blood pressure (mmHg) | 133.0 ± 26.9 | | 137.1 ± 25.3 | | 130.9 ± 27.5 | | < 0.0001 |
| Diastolic arterial blood pressure (mmHg) | 73.8 ± 15.6 | | 74.8 ± 14.5 | | 73.0 ± 15.9 | | 0.0029 |
| Systolic<90mmHG or diastolic<60mmHg | 526 | 16.6 | 117 | 13.1 | 351 | 18.3 | 0.0006 |
| Impaired consciousness or abnormal mental status | 503 | 15.9 | 9 | 1.0 | 448 | 23.4 | < 0.0001 |
| Chest X-ray | | | | | | | |
| Local infiltrate | 2013 | 63.8 | 570 | 63.7 | 1252 | 65.6 | 0.4012 |

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| | | | | | | | |
|----------------------------------|------|------|-----|------|------|------|--------------------|
| Pleural effusion or collection | 179 | 5.7 | 43 | 4.8 | 117 | 6.1 | 0.1661 |
| CRB-65 (no of points) | | | | | | | |
| 0 | 726 | 22.9 | 233 | 26.0 | 403 | 21.0 | < 0.0001 |
| 1 | 1299 | 41.0 | 477 | 53.3 | 667 | 34.8 | |
| 2 | 848 | 26.8 | 166 | 18.5 | 596 | 31.1 | |
| 3 | 251 | 7.9 | 16 | 1.8 | 216 | 11.3 | |
| 4 | 42 | 1.3 | 3 | 0.3 | 35 | 1.8 | |
| Site of care | | | | | | | |
| Non admitted | 518 | 16.5 | 200 | 22.4 | 249 | 13,1 | < 0.0001 |
| Admission in medicalwards | 2295 | 72.9 | 656 | 73.5 | 1386 | 72.9 | |
| Admitted in intensive care units | 335 | 10.6 | 37 | 4.1 | 266 | 14.0 | |
| Antimicrobialtherapyat ED | 3148 | | | | | | |
| Parenteral | 2285 | | 674 | 75.7 | 1611 | 86.6 | < 0.0001 |
| Oral intake | 467 | | 217 | 24.4 | 250 | 13.4 | |
| | | | | | | | |
| 0-4 hours | 1424 | | 419 | 49.7 | 1005 | 56.0 | 0.0025 |

Table 3: Baseline Characteristics of the Study Population and Comparison of Study Groups According to Adherence to 2010 Guidelines for First Line Antimicrobial Agents in Community-Acquired Pneumonia. Results are presented as number (percent %) and mean (standard deviation) as indicated. Boldface for p values indicates significant result.

Description of antimicrobial therapy in the ED

Of the 3.166 patients, 2.812 (89%) received antimicrobial agents during their ED stay (Figure 1, Table 4). Median delay to first antibiotic administration in the ED was 3hrs 45min (3hrs 12min), and treatment consisted in a single agent in 1.946 (71%), two agents in 794 (29%) and three agents in 18 (6%). Antibiotics prescribed were mostly β -lactams (n=2.546, 90%). A majority of patients (1297, 46%) received amoxicillin-clavulanate. Seven hundred and twenty seven patients (23%) had received antibiotics prior to ED visit. We observed that 354 (11%) did not receive antimicrobial agents during their ED stay. These patients were distributed as follow: 54 in group 1, 140 in group 2, 9 in group 3, 3 in group 4, 108 in group 5 and 40 in group 6. Of these 354 patients, 127 (36%) had received antibiotics before ED visit.

| Patients' groups | Definition of groups | Antimicrobial therapy | Adherence to antibiotic guidelines N (%) |
|------------------------|--|-----------------------------|---|
| Total N=2 812 | Total | Adherence | 895 (31.8) |
| Group 1 N=339 | Age <65 years | Adherence | 122 (36.0) |
| | | Amoxicillin | 96 |
| | | Pristiniamycin | 5 |
| | | Telithromycin | 10 |
| | | Macrolid | 11 |
| Group 2 N=1 063 | Age < 65 years and underlying disorders or Age >= 65 years | Adherence | 711 (66.9) |
| | | Amoxicillin-clavulanic acid | 481 |
| | | Levofloxacin | 52 |
| | | Cefotaxim | 19 |
| | | Ceftriaxon | 159 |

| | | | |
|----------------------|---|-----------------------------|------------------|
| Group 3 N=53 | Seasonal influenza and Age <65 years | Adherence | 22 (41.5) |
| | | Amoxicillin-clavulanic acid | 18 |
| | | Pristiniamycin | 3 |
| | | Telithromycin | 1 |
| Group 4 N=34 | Seasonal influenza and Age < 65 years and underlying disorders or Age >= 65 years | Adherence | 22 (64.7) |
| | | Amoxicillin-clavulanic acid | 18 |
| | | Levofloxacin | 1 |
| | | Cefotaxim | 2 |
| | | Ceftriaxon | 1 |
| Group 5 N=978 | Symptoms of severity | Adherence | 18 (1.8) |
| | | Ceftriaxon + Macrolid | 0 |
| | | Cefotaxim + Macrolid | 18 |
| | | Ceftriaxon + Levofloxacin | 0 |
| | | Cefotaxim + Levofloxacin | 0 |
| Group 6 N=345 | Symptoms of severity and COPD or cystic fibrosis | Adherence | 0 (0.0) |
| | | Anti-Pseudomonas b-lactam | 0 |
| | | + Aminoglycosid + Macrolids | |

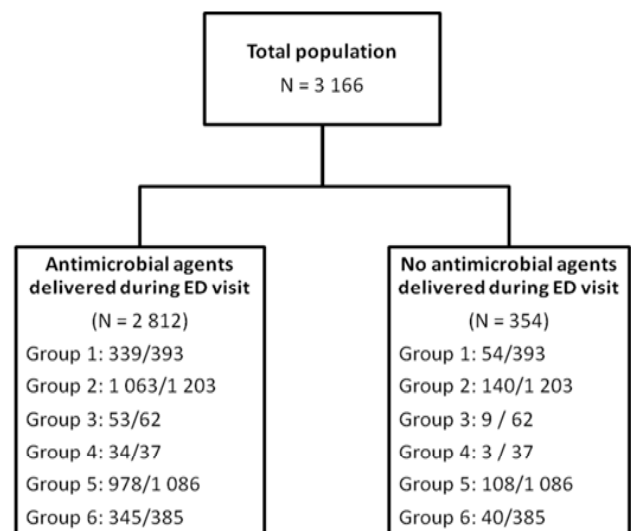
Table 4: Adherence to antibiotic guidelines for community-acquired pneumonia in patients receiving antibiotics in the ED with respect to patients' groups.

Figure 1: Chart flow of the study population of CAP patients with respect to delivery of antimicrobial agents during their visit in the emergency department. ED: emergency department; group 1: CAP patients <65 years without signs and symptoms of severity; group 2: CAP patients <65 years with significant underlying disorders and >65 years without signs and symptoms of severity; group 3: CAP patients < 65 years during seasonal flu without signs and symptoms of severity; group 4: CAP patients < 65 years with significant underlying disorder and >65 years during seasonal flu without signs and symptoms of severity; group 5: CAP patients without COPD and cystic fibrosis; group 6: CAP patients with COPD and cystic fibrosis and symptoms of severity.

Adherence to antibiotic guidelines

Adherence to antibiotic guidelines (summarized in Table 1) was observed in 895 patients with suspected CAP (28%). Adherence widely differed between patients' categories, ranging from 0 (group 6) to 66.9% (group 2) (Table 4). In a multivariate model, we determined factors that influenced adherence to guidelines (Table 5). Coexistence of COPD, congestive heart failure, and patients aged 65 and older were associated with non-adherence to antibiotic guidelines. Patients were more likely to receive antimicrobial therapy according to antibiotic guidelines. Respiratory

rate, decreased blood pressure and impaired consciousness were more frequent in patients receiving antimicrobial therapy in accordance with guidelines. This was also observed in patients admitted in medical wards and intensive care units. Of note, results of chest X-rays did not influence adherence to antibiotic guidelines.



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| | Unadjusted models | | | Adjusted and final model* | | |
|--|-------------------|---------------|--------------------|---------------------------|---------------|--------------------|
| | OR | 95% CI | p | OR | 95% CI | p |
| Age >= 65 years | 0.75 | [0.63 ; 0.89] | 0.0007 | 0.48 | [0.39 ; 0.60] | 0.0012 |
| COPD | 0.80 | [0.66 ; 0.97] | 0.0230 | 0.77 | [0.62 ; 0.95] | < 0.0001 |
| Congestive heartdisease | 0.84 | [0.71 ; 1.01] | 0.0595 | 0.79 | [0.64 ; 0.98] | 0.0163 |
| Antimicrobial agents within 7 days | 1.29 | [1.05 ; 1.57] | 0.0138 | 1.29 | [1.04 ; 1.60] | 0.0337 |
| Pulse oxymetry< 90% (room air) | 0.47 | [0.40 ; 0.56] | <0.0001 | 0.70 | [0.57 ; 0.86] | 0.0229 |
| >= 30 cycles / min | 3.95 | [3.10 ; 5.04] | < 0.0001 | 3.50 | [2.69 ; 4.56] | 0.0007 |
| Systolic<90mmHG or diastolic<60mmHg | 1.49 | [1.19 ; 1.87] | 0.0005 | 1.33 | [1.03 ; 1.71] | < 0.0001 |
| Impaired consciousness or abnormal mental status | 30.01 | [15.43;58.35] | <0.0001 | 28.78 | [14.71; 56.1] | 0.028 |
| Site of care | | | | | | |
| Non admitted | Reference | | | Reference | | |
| Admitted in medicalward | 1.70 | [1.38 ; 2.09] | <0.0001 | 1.77 | [1.38 ; 2.26] | < 0.0001 |
| Admitted in intensive care units | 5.77 | [3.90 ; 8.53] | <0.0001 | 3.72 | [2.40 ; 5.76] | < 0.0001 |

Abbreviations: OR Odds ratio; CI Confidence Interval
*variables included in the model before the stepwise backward selection : Male sex, age >= 65 years, nursing home resident, COPD, liver disease, congestive heart disease, cerebrovascular disease, chronic renal disease, active neoplasm, hospitalization during year, unfavorable social conditions, unsatisfactory compliance, antimicrobial agents within 7 days, pulse oxymetry <90%, >=30 cycles/min, systolic <90 mmHG and diastolic <60 mmHg, impaired consciousness or abnormal mental status, pleural effusion or collection, site of care, antimicrobial therapy at ED.

Table 5: Unadjusted and adjusted final models of multivariate analysis of factors that influence non adherence to 2010 Guidelines for First Line Antimicrobial Agents in Community-Acquired Pneumonia. Results are presented as odds ratio (OR) and their 95% confidence interval (95%CI) and corresponding P values.

Discussion

Here we report the largest audit for CAP management in the emergency department conducted in France. We observed that

- Antimicrobial therapy often differed from guidelines in patients visiting the ED with CAP,
- Adherence to antibiotic guidelines widely differed between patients' categories, and
- Adherence to antibiotic guidelines was negatively associated with significant underlying disorders and SpO₂, and positively associated with age, other signs and symptoms of severity and admission.

A recent audit described current management of CAP in UK hospitals [7]. Authors observed that most of the 64 units had local CAP guidelines derived from national recommendation. The results from the present study may differ as we focused on initial management in the ED. Indeed most authors emphasize the importance of the very first hours of CAP management that significantly influence outcome. The British Thoracic Society (BTS) audit focused on global management whereas we decided to spe-

cifically identify initial decision processes. Consequently, we assessed initial management and immediate death in the ED. Thus, we observed that 1% CAP patients died in the ED, whereas 3.7% patients died at day 1 in the British study. Median age of the CAP patients recorded in recent trial is usually 70 years. It was 76 in the BTS audit [7]. In our study, half patients were 75 or older. In addition, significant underlying disorders were frequently encountered in our population. Approximately a quarter suffered from congestive heart failure, more than 20% had COPD and active neoplasm was recorded in 12%. These characteristics are close from those of recent assays conducted in the ED [8]. Therefore, our population corresponds to current descriptions in terms of age and comorbidities.

Adherence to guidelines is usually perceived as a better quality of treatment, improving survival, hospital length of stay and readmission rate [9]. It has been reported that patient prognosis improves when antibiotics are concordant to guidelines [10]. Here we report that few ED patients received antimicrobial therapy according to current guidelines. Studies have reported that adherence to CAP antibiotics guidelines can be satisfactory without any intervention [11]. Attempts to improve adhesion to guidelines have

mostly been efficient. The British audit reported satisfactory adherence, i.e. 50-70%, based upon local recommendation derived from BTS guidelines [7]. This probably corresponds to the optimal level of adherence expected. Indeed, guidelines have to be overruled in specific case including recent travels, epidemic contexts, and previous antimicrobial therapy. In our study, 23% received antibiotics prior to ED visit. Conversely to previous publications, our data included outpatients, i.e. patients discharged after their ED visit. Patients with CRB65 score at 0 are usually treated as outpatients. These represented 22.9% of our study population. Including this population could merely explain the discrepancy of our results. In our study, CBR65 classification did not influence adherence to antibiotic guidelines. We even observed in a univariate analysis that lower CRB65 score were associated with better compliance to antibiotic guidelines. Evaluation of CAP patients is complex. It can be assumed that emergency physicians sometimes simplify CAP patient's evaluation to decide anti-biotherapy. As a matter of fact, French recommendations propose to distribute CAP patients in different 6 classes. This may be difficult to apply at bedside in the ED. We observed that ED physicians mostly prescribed amoxicillin-clavulanate to CAP patients. Therefore, patients from group 1 received antibiotics with broader spectrum than suggested by guidelines and group 5 received antibiotics with too narrow spectrum. Similarly, intravenous antibiotics and dual therapy were overused in patients with low severity CAP. This suggests that most ED physicians use a simplified strategy to prescribe antibiotics. Consistently previous studies suggest to simplify antimicrobial treatment even in more severe CAP patients [12] another hypothesis is that implementation of antibiotics guidelines should be actively accompanied. A controlled trial demonstrated that local recommendations should be sustained by specific tutorial measures and practices feedback [13]. When unsatisfactory appliance of antibiotic guidelines is observed, it should be considered if these guidelines have been correctly diffused to caregivers, if they have been implemented in local recommendations, if they fit patient's and physicians' needs, if they add any benefit as compared to previous practices. In case there is no evidence for these, the whole process should be carefully re-assessed.

Both the adherence to CAP guidelines and the time to first antibiotic have been associated with clinical outcome [2]. In the British audit, 58% of patients received their first antibiotic within 4 h of hospital admission [7]. We observed that half patients received the first dose within 3h45. Whereas this result may be perceived as unsatisfactory, it has been suggested that a strategy based on delays may alter appropriate antimicrobial treatments [14].

Patients with CAP frequently suffer from underlying disorders and ageing, factors that increase diagnosis' uncertainty and quality of antimicrobial therapy [4,15]. Many patients of our pop-

ulation were elderly and presented with comorbidities. To note, chest X-ray frequently lacked typical parenchymal infiltrates, a cornerstone result to help diagnosis frequently reported in such patients [15]. Patients presenting to the ED with clinical signs of CAP and inconclusive chest X-ray frequently suffer from CAP [5]. Ascertaining diagnosis may significantly improve diagnosis and treatment of CAP patients. Indeed, in a recent publication, multidetector CT-scan revealed a parenchymal infiltrate in 33% of patients without infiltrate on chest X-ray and excluded CAP in 29.8% of patients with parenchymal infiltrate on X-ray and alters prescription of antimicrobial agents by ED physicians. This may partly explain our results as ED physicians had to include unselected patients with suspected CAP.

Limitations

This study suffers from limitations. Patients were included if the emergency physician suspected a CAP based on his/her usual practice and own judgment. We used a numeric scale (1-10) to evaluate ED physicians' certainty for diagnosis of CAP (data not shown). We observed that diagnosis of CAP was uncertain in a majority of patients with suspected CAP. Several studies suggest that diagnosis of CAP remains despite clinical examination, biomarkers results and X-rays [16,17]. This raised the concern about definition of CAP in the ED, especially in older patients with less specific signs and symptoms [18]. Another questionable approach might be the exclusion of patients that did not receive antimicrobial therapy for the analysis of adherence to antibiotic guidelines. We did not capture reasons why antimicrobial treatment was delayed or suspended in 354 (11%) patients visiting the ED with suspected CAP. This could be related to prior antimicrobial therapy (727 patients, 23%), uncertain diagnosis, advice of a specialist in infectious disease. Therefore, we decided to exclude these patients from the analysis. Of note, patients since 15 years of age were included in our study whereas they may be considered as non-adults. However, pathogens responsible for CAP don't differ between these patients and young adults, and a category with patients of patients aged 15 to 19 years appears in epidemiological studies [19]. We included only 25 (0.8%) patients aged 15 to 18. In addition, our aim was to describe management of CAP in French emergency departments. Therefore we were unable to determine if treatments and site-of-care decided by ED physicians altered patients' outcome. Indeed 13% patients were discharge whereas 21% were scored 0 according to CRB65, as recommended by the French CAP guidelines. This apparent over-admission rate may be balanced by the benefit of clinical sense that detects patients with latent organ failure and unfavorable outcome [20]. Indeed, patients from the PORT cohort with a low Pneumonia Severity Index were more likely to die if they were admitted. This basically suggested that physicians were able to detect CAP patients with risk of adverse outcome de-

spite low severity score. Finally, we were unaware to subsequent admissions for CAP patients at each center.

Conclusion

Here we report that adherence to antibiotic guidelines is low in CAP patients that visit French ED. Whereas efforts are warranted to improve, complexity of antibiotic guidelines may contribute to this unsatisfactory adherence.

References

1. Waterer GW, Rello J, Wunderink RG (2011) Management of community-acquired pneumonia in adults. *Am J Respir Crit Care Med* 183: 157-164.
2. Houck PM, Bratzler DW, Nsa W, Ma A, Bartlett JG (2000) Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. *Arch Intern Med* 164: 637-644.
3. [Antibiothérapie par voie générale dans les infections respiratoires basses de l'adulte. Pneumonie aiguë communautaire Exacerbations de Bronchopneumopathie Chronique Obstructive.] http://www.infectiologie.com/site/medias/_documents/consensus/2010-infVRB-spilf-afssaps.pdf. Last access 10th of June, 2014.
4. Metlay J, Schulz R, Li YH, Singer D, Marrie T et al. (1997) Influence of age on symptoms at presentation in patients with community-acquired pneumonia. *Arch Intern Med* 157: 1453-1459.
5. Claessens YE, Debray MP, Tubach F, Brun AL, Rammaert B et al. (2015) Early Chest CT-Scan to Assist Diagnosis and Guide Treatment Decision for Suspected Community-Acquired Pneumonia. *Am J Respir Crit Care Med* 192: 974-982.
6. Kanwar M, Brar N, Khatib R, Fakhri M (2007) Misdiagnosis of community-acquired pneumonia and inappropriate utilization of antibiotics: side effects of the 4-h antibiotic administration rule. *Chest* 131: 1865-1869.
7. Wei Shen Lim WS, Woodhead M (2011) British Thoracic Society adult community acquired pneumonia audit 2009/10. *Thorax* 66: 548-549.
8. Schuetz P, Christ-Crain M, Thomann R, Falconnier C, Wolbers M et al. (2009) Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial. *JAMA* 302: 1059-1066.
9. Dean NC, Bateman KA, Donnelly SM, Silver MP, Snow GL et al. (2006) Improved clinical outcomes with utilization of a community-acquired pneumonia guideline. *Chest* 130: 794-799.
10. Mortensen EM, Restrepo MI, Anzueto A, Pugh JA (2006) Antibiotic therapy and 48-hour mortality for patients with pneumonia. *Am J Med* 119: 859-864.
11. Capelastegui A, España PP, Quintana JM, Gorordo I, Ortega M et al. (2004) Improvement of process-of-care and outcomes after implementing a guideline for the management of community-acquired pneumonia: a controlled before-and-after design study. *Clin Infect Dis* 39: 955-963.
12. Marrie TJ, Lau CY, Wheeler SL, Wong CJ, Vandervoort MK et al. (2000) A controlled trial of a critical pathway for treatment of community-acquired pneumonia. CAPITAL Study Investigators. Community-Acquired Pneumonia Intervention Trial Assessing Levofloxacin. *JAMA* 283: 749-755.
13. Yealy DM, Auble TE, Stone RA, Lave JR, Meehan TP et al. (2005) Effect of increasing the intensity of implementing pneumonia guidelines: a randomized, controlled trial. *Ann Intern Med* 143: 881-894.
14. Metersky ML, Sweeney TA, Getzow MB, Siddiqui F, Nsa W et al. (2006) Antibiotic timing and diagnostic uncertainty in Medicare patients with pneumonia: is it reasonable to expect all patients to receive antibiotics within 4 hours? *Chest* 130: 16-21.
15. Mandell LA, Wunderink RG, Waterer GW (2015) Community-acquired pneumonia. *N Engl J Med* 372: 293-294.
16. Van Vugt SF, Broekhuizen BD, Lammens C, Zuithoff NP, de Jong PA et al. (2013) Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study. *BMJ* 346: f2450.
17. Syrjälä H, Broas M, Suramo I, Ojala A, Lähde S (1998) High-resolution computed tomography for the diagnosis of community-acquired pneumonia. *Clin Infect Dis* 27: 358-363.
18. Metlay J, Schulz R, Li YH, Singer DE, Marrie TJ, Coley CM et al. (1997) Influence of age on symptoms at presentation in patients with community-acquired pneumonia. *Arch Intern Med* 157: 1453-1459.
19. Metersky ML, Masterton RG, Lode H, File TM Jr, Babinchak T (2012) Epidemiology, microbiology, and treatment considerations for bacterial pneumonia complicating influenza. *Int J Infect Dis* 16: e321-331.
20. Labarere J, Stone RA, Obrosky DS, Yealy DM, Meehan TP et al. (2007) Comparison of outcomes for low-risk outpatients and inpatients with pneumonia: a propensity adjusted analysis. *Chest* 131: 480-488.