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Implementation of an Empirical Treatment Protocol for Community-Acquired Pneumonia in a Social–Health Care Hospital †

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Abstract: Community-acquired pneumonia (CAP) is a common acute infection associated with significant morbidity and mortality, particularly in older adults with significant comorbidities. For this reason, an empirical treatment protocol for CAP was developed in a social–health care hospital. The aim of the study was to evaluate compliance with this protocol. Methods: a descriptive, retrospective study of all patients admitted to our hospital and diagnosed with CAP from September to December 2022 was conducted. Demographic variables: age, sex; pharmacological variables: empirical antibiotic treatment according to protocol, change of antibiotic treatments, mean duration of treatment, compliance with criteria and performance of sequential therapy on the third day and after the third day. Results: 55 patients were included (mean age, 88.9 years (64–103), 58.2% men). A total of 50.9% received empirical antibiotic treatment according to the protocol. The empirical antibiotics prescribed were amoxicillin/clavulanate (25.5%), ceftriaxone + levofloxacin(23.6%), piperacillin/tazobactam (18.2%), ceftriaxone (14.5%), levofloxacin (7.3%), meropenem(5.5%), ertapenem (1.8%), imipenem (1.8%) and levofloxacin + azithromyzine (1.8%). Change of antibiotics occurred in 27.3%, and the mean duration of treatment was 8.3 days. Sequential therapy: 56.4% met the criteria on day 3, but this was only among 19.3%. Of the remaining patients, 22.45% were switched to oral in an average of 6 days. Conclusion: compliance with the empirical treatment protocol in CAP occurred in a very low percentage of patients. Moreover, in patients who met the criteria for sequential therapy, it was performed after the third day. Therefore, with the aim of improving these results, new measures and activities have been proposed.

Keywords: CAP; empirical treatment; sequential therapy

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1. Introduction

CAP is defined as an acute community-acquired infection as opposed to the hospital-acquired (nosocomial) infection of the lung parenchyma. It is a common and potentially serious disease associated with significant morbidity and mortality, particularly in older adults and those with significant comorbidities [1,2].

The etiology is conditioned by several aspects such as comorbidity, baseline functional status, severity of the acute episode, antimicrobial treatments received and contact with the hospital system or place of residence. Although, in most cases, the microorganism causing CAP is unknown, *Streptococcus pneumoniae* is the bacterium mainly identified in most studies [1–3]. However, in recent years, its detection has decreased significantly. In

contrast, the detection of viruses has increased considerably since the COVID-19 pandemic, and they have already been detected in approximately one third of community-acquired pneumonias [2]. Atypical pathogens (*Mycoplasma pneumoniae, Haemophilus influenza, Legionella* spp. and *Chlamydophila pneumoniae*) are not usually identified in clinical practice due to a lack of standardized, rapid or specific tests, with the exception of Legionella pneumophila. In addition, with increasing age, the frequency of these microorganisms decreases, and the incidence of Haemophilus influenza pneumonia and Gram-negative bacilli increases.

The incidence of CAP in adults is approximately 5.16 to 7.06 cases per 1000 inhabitants/year, a rate that increases with age, reaching 25 to 35 cases per 1000 inhabitants/year in the population over 65 years of age [1,2]. In this population group, it is also a frequent cause of urgent care and hospital admission.

This high incidence has been related to physiological changes associated with aging in the respiratory and immune systems, together with the greater probability of clinical and social situations (dysphagia, malnutrition, institutionalization) and chronic diseases that accumulate with age. All these factors make the elderly more vulnerable to the development of infections and, more specifically, pneumonia, as well as to an increased risk of a worse outcome [1,2].

Given the high prevalence and important clinical and health consequences, CAP in the elderly is considered a major health problem.

For this reason, the Infection, Prophylaxis and Antibiotic Policy Committee of our healthcare center developed a protocol for the diagnosis and empirical treatment of CAP. The protocol (Table 1) includes the empirical antibiotic treatment to be followed in the different CAP syndromes (typical, atypical, aspiration and immunocompromised patients), including patients allergic to penicillin, with the most frequent microorganisms and the duration of treatment [3–5].

Table 1. CAP empirical antibiotic treatment protocol.

Syndrome	Common Etiologies	Empirical Treatment	Duration
Community-acquired pneumonia (general)	Typical: *S. pneumoniae* *H. influenzae* (>65 years or comorbidity) *S. aureus*	(a) Typical: Ceftriaxone 2 g/24 h IV o Amoxicillin/clavulanic acid 1–2 g/8 h IV	5 days if favorable evolution Prolong if: - Slow response - Comorbidity - Empyema - Atypical
	Atypical: *M. pneumoniae* *C. pneumoniae* *C. burnetti* *Legionella* Virus	(b) Atypical or suspected *Legionella*: As in typical and add Azithromycin 500 mg/24 h v.o. * o Monotherapy with Levofloxacin 500 mg/12 h IV (first day) followed by 500 mg/24 h IV	
		(c) Allergic Levofloxacin 500 mg/12 h IV (first day) followed by 500 mg/24 h IV	
Community Pneumonia (aspiration * and pulmonary abscess) * Consider in patients with swallowing disorders or altered levels of consciousness, alcoholism and/or septic mouth	Anaerobes, microorganisms present in the oral cavity	Amoxicillin/clavulanic acid 2 g/8 h IV O Ceftriaxone 2 g/24 h IV (b) Allergic: Levofloxacin 500 mg/12 h IV (first day) followed by 500 mg/24 h IV + Clindamycin 600–900 mg/8 h IV	7–10 days (discontinue in 48–72 h if no infiltrate is observed after an aspiration episode) Prolong if: - Extensive - Slow response - Lung abscess (weeks) - Pleural effusion

Table 1. *Cont.*

Syndrome	Common Etiologies	Empirical Treatment	Duration
Community-acquired pneumonia in immunocompromised patients	Those of CAP in the general population and in addition: *P. aeruginosa* It may be necessary to consider (according to context): - *Nocardia* spp. - *Rhodococcus* spp. - Tuberculosis - Fungi - (*Pneumocystis*) - Viruses (respiratory, CMV)	Piperacillin/tazobactam 4 g/6 h IV +Azithromycin 500 mg/24 h O Cefepime 2 g/8 h IV (caution in the elderly with impaired renal function, risk of encephalopathy) + Azithromycin 500 mg/24 h If neutropenia or clinical severity, add: Amikacin 15 mg/kg/24 h Allergic: Aztreonam 2 g/8 h IV + Levofloxacin 500 mg/12 h IV (first day) followed by 500 mg/24 h IV O Levofloxacin 500 mg/12 h IV (first day) followed by 500 mg/24 h IV + Tigecycline 50 mg/12 h IV (initial dose 100 mg) If bilateral interstitial involvement, also consider *Pneumocystis jirovecii* and add: Cotrimoxazole 15 mg/kg/day IV (trimethoprim component) divided in 3–4 doses. Add Methylprednisolone 40 mg/12 h IV if $PaO_2 < 70$	Risk of *P. aeruginosa* - Prolonged systemic corticosteroid treatment - Frequent (>4 times/year) or recent administration of antibiotics (in the last 3 months) - Severe COPD (FEV1 < 30%) - Clinically significant bronchiectasis - Nasogastric tube for enteral feeding - ICU admission

* Azithromycin has not been shown to be inferior to quinolones (mortality, length of stay…) in *Legionella pneumonia*, and in the case of severe pneumococcal pneumonia, it may provide added clinical benefits independent of pneumococcal sensitivity profile.

The aim of the study was to evaluate compliance with this protocol in order to reduce the incidence of multidrug-resistant germs and improve the use of antibiotics in the hospital.

2. Methods

A descriptive, retrospective study of all patients admitted to the hospital with a diagnosis of CAP from September to December 2022 was conducted.

The variables collected were demographic variables: age, sex; microbiological variables: sputum culture collection; pharmacological variables: empirical antibiotic treatment prior to admission, empirical antibiotic treatment according to protocol, change of antibiotic treatments, mean duration of treatment, compliance with criteria and performance of sequential therapy on the third day and after the third day.

Data were collected from the electronic medical record.

3. Results and Discussion

Fifty-eight patients were admitted with a diagnosis of CAP, of which three were excluded because the actual diagnoses were nosocomial pneumonia and urinary tract infections. Finally, 55 patients were included with a mean age of 88.9 years (64–103), 58.2% being male. A sputum culture was only collected in four patients whose result was commensal flora.

Antibiotic treatment prior to admission was received by 43.6% of patients, and empirical antibiotic treatment was prescribed according to protocol in 50.9% of patients.

The empirical antibiotics prescribed are presented in Table 2.

In total, 27.3% of the patients underwent antibiotic replacement, and the mean duration of treatment was 8.3 days.

Regarding sequential therapy, 56.4% of the patients met the criteria on the third day of treatment, but only 19.3% of them did so. Of the remaining patients, antibiotic treatment was switched to the oral route before completion in only 22.45% in an average of 6 days.

For protocol development, we based our protocol on protocols [4,5] from other hospitals, of which the main microorganism causing CAP is also *S. pneumonia* [6,7]. In one of them, for the prescription of an empirical treatment, they first differentiate between CAP in patients without

admission criteria and those with admission criteria, with the same empirical treatment as our protocol [6]. In the case of CAP due to witnessed bronchoaspiration, they do not recommend the use of prophylactic antibiotics, since they have not been shown to reduce mortality or prevent complications [6,8]. In the case of aspiration and lung abscess and/or an immunocompromised patient, empirical antibiotic treatment is required [6].

Table 2. Empirical antibiotics prescribed.

Empirical Antibiotic Prescribed	Number of Patients	Percentage of Patients (%)
Amoxicillin/Clavulanic acid	14	25.5
Ceftriaxone + Levofloxacin	13	23.6
Piperacilin/Tazobactam	10	18.2
Ceftriaxone	8	14.5
Levofloxacin	4	7.3
Meropenem	3	5.5
Ertapenem	1	1.8
Imipenem	1	1.8
Levofloxacin + Azithromyzine	1	1.8

In another hospital, as an empirical treatment for general CAP in patients not allergic to penicillin, only ceftriaxone or levofloxacin is proposed. This is in contrast to our center, which proposes a choice between ceftriaxone and amoxicillin/clavulanic acid, reserving levofloxacin for CAP with suspected atypical disease [9]. In addition, the EMA and the AEMPS have issued alerts about the use of fluoroquinolones due to the occurrence of severe, long-lasting, disabling and potentially irreversible adverse reactions affecting mainly the musculoskeletal and nervous systems. As a result, the EMA significantly restrict their use in 2019 [10].

In a third protocol reviewed, the empirical treatment of choice in the case of general CAP is levofloxacin and, alternatively, ceftriaxone or amoxicillin/clavulanic acid + clarithromycin. In patients with risk factors, it is piperacillin/tazobactam together with an aminoglycoside (amikacin or tobramycin) [11]. In the case of patients with a history of pulmonary aspiration, amoxicillin/clavulanic acid or ertapenem is proposed as the first choice. In our case, we do not recommend treatment with carbapenems in order to reserve them for severe infections caused by multi-resistant microorganisms and to avoid increasing antibiotic resistance [11].

The fact that different treatment protocols exist in each hospital, together with the fact that physicians rotate through several hospitals during their professional career, makes compliance with these protocols difficult, since an antibiotic for a specific indication may be the antibiotic of choice in one hospital but not in the rest of the hospitals.

In addition, we have not found results of compliance with these protocols in the empirical treatment of CAP in other hospitals, so we cannot compare ourselves on compliance with these protocols.

When prescribing antibiotics in elderly patients, the probable microbial etiology, the severity of the patient and the characteristics of the possible antibiotics to be used must be taken into account. Due to the difficulty in the etiological diagnosis of CAP, an empirical treatment must be indicated in most cases [2].

The implementation of the protocol for the diagnosis and empirical treatment of CAP aims to standardize the use of diagnostic tests and the empirical use of antibiotics in elderly patients in order to achieve a better use of antibiotics [6,7]. However, in our center, compliance with the protocol in the choice of empirical treatment occurred in a very low percentage of patients with a treatment duration longer than indicated in the treatment plan. Moreover, of the patients who met the criteria for sequential therapy on the third day of antibiotic treatment, it was carried out in very few. It was carried out in a higher percentage of patients in an average of 6 days.

Due to the results obtained, new improvement measures have been proposed, such as: conducting training sessions on empirical treatment of CAP in the hospital, creating protocols for the empirical treatment of the different types of CAP (including for patients with penicillin allergy) in the electronic prescription program (Farmatools®.Spain), together with the configuration of alert systems for the number of days of treatment, to facilitate compliance with the protocol both in the choice of the appropriate antibiotic and the duration of treatment. Finally, it has been proposed to change the indicator of sequential therapy on the third day to the fifth day of antibiotic treatment, since due to the type of patients in our center, it is possible that the third day is too early to switch from intravenous to oral therapy.

It will be necessary to carry out a new study after the implementation of these new measures to check if they have been effective and if we have managed to improve the results of compliance with the protocol.

4. Conclusions

There is low compliance with the CAP empirical treatment protocol in the social–health center, both with the choice of empirical antibiotic and its duration, as well as with the use of sequential therapy. Therefore, it is necessary to implement new measures to improve compliance and to reduce the incidence of multidrug-resistant germs.

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