ORIGINAL ARTICLE

Uncomplicated community-acquired pneumonia in immunocompetent children

Stephanie Schafer[1], Valentina Chakr[2], Gabriela Petitot[2]

Abstract

Pneumonia is one of the leading causes of mortality in children outside the neonatal period. Its prevalence has been reduced in recent years mainly due to the implementation of vaccines against *S. pneumoniae* and H. influenzae type b. The main causative pathogens vary according to the age group, with pneumococcus being a prevalent agent in children from 2 months of age. There are no specific symptoms and radiological pathognomonic signs of pneumonia. Initial chest radiographs may appear normal and the presence of changes does not differentiate between bacterial and viral causes. Images should be performed in hospitalized patients and is not necessary for outpatients. Other imaging studies have emerged as an option for diagnostic assistance, such as thoracic ultrasonography and pulmonary magnetic resonance imaging. Laboratory tests should be restricted to inpatients and the result should be interpreted within the clinical context and other complementary tests. Isolation of the etiologic agent is useful for correct therapeutic management and to reduce bacterial resistance rates. However, the sensitivity of these tests remains low and it is necessary to start treatment according to the most prevalent bacteria, according to the age group and the vaccination state. The most frequent antimicrobial agents used in inpatient and outpatient settings are penicillin and amoxicillin. In case of suspicion of atypical pneumonia, macrolides should be used.

[1] Hospital de Clínicas de Porto Alegre, Serviço de Pediatria - Porto Alegre - Rio Grande do Sul - Brasil.
[2] Universidade Federal do Rio Grande do Sul, Departamento de Pediatria - Porto Alegre - Rio Grande do Sul - Brasil.

Correspondence to:
Stephanie Schafer.
Hospital de Clínicas de Porto Alegre - Porto Alegre - Rio Grande do Sul - Brasil. Rua Ramiro Barcelos, nº 2350, Santa Cecilia, Cidade, Porto Alegre - RS, Brazil.
CEP: 90035-007. E-mail: tephi.schafer@gmail.com

INTRODUCTION

Pneumonia (PNM) is an important cause of morbidity and mortality in children off the neonatal period[1-4].

The incidence and severity of childhood pneumonia have declined in recent decades (Figure 1) due to improved access to healthcare services, population socioeconomic conditions, and vaccine development and application, particularly *Streptococcus pneumoniae* and *Haemophilus influenza*-type b vaccines[1,5]. Despite the reduction in hospitalization rates after vaccine introduction, studies have shown an increase in cases of complicated pneumonia caused by *S. pneumoniae*, especially serotypes 1, 3, 5 and 19A, in recent years[4].

The main risk factors for mortality from childhood pneumonia are malnutrition, non-breastfed children, crowded housing, exposure to household pollution and low birth weight[1,6].

PATHOPHYSIOLOGY

Pneumonia is characterized by inflammation of the lung tissue caused by an infectious agent.[7] The lower respiratory tract is not a sterile environment, and pneumonia may be due to an imbalance (dysbiosis) in the respiratory tract microbiota resulting from factors related to the host, environment and pathogen (s)[1].
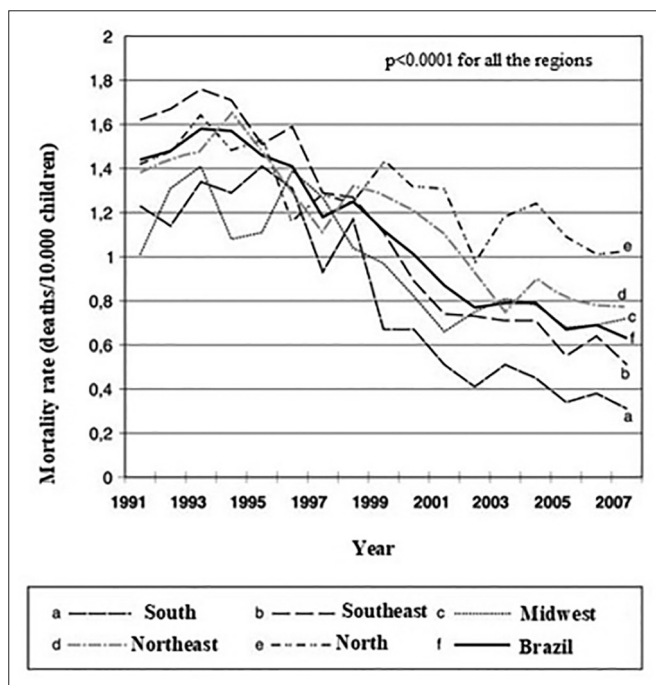

Figure 1. Pneumonia-associated mortality reduction in children < 5 years in Brazil and demographic regions.

ETIOLOGY

Identifying the cause of PNM is important to guide treatment, to develop clinical recommendations for empirical treatment, and to assess the impact of preventive interventions (vaccines). However, it is not simple to define the etiology of PNM, because the disease may have multiple pathogens, because bacteria rarely invade sterile sites (blood), and because it is difficult to distinguish colonizing flora from pathogenic organisms (molecular tests). It is difficult to get a representative sample of the lower airway, and contamination with *S. pneumoniae* and *H. influenzae*, which are pathogenic bacteria but colonizers of the upper airway, is likely to occur[1].

S. pneumoniae is assumed to be the most frequently associated agent with bacterial PNM, accounting for 1/3 of the cases[4]. Other pathogens are: *H. influenzae*, *M. catarrhalis*, S. Group A aureus and streptococcus. The latter two most often develop into severe conditions and/or empyema[7-11].

Atypical germs (*Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*) are most commonly related to older children (> 4 years). They often cause more gradual onset PNM, accompanied by headache, malaise, dry cough, sore throat, otitis media, and low fever (or no fever). Extra pulmonary symptoms may occur (encephalitis, aseptic meningitis, neuropathy, urticaria, purpura, etc.)[7-9,11,12].

Viruses are a major cause of pneumonia in younger children (< 2-5 years), with respiratory syncytial virus being the main agent. Other pathogens are: rhinovirus, influenza, parainfluenza, adenovirus, varicella virus, cytomegalovirus, enterovirus, herpes, metapneumovirus, bocavirus and coronavirus. About 1/3 to 45% of cases may have bacterial coinfection, with *S. pneumoniae* being the most frequently involved bacterium[4,7-9]. Table 1 shows the main pathogens associated with pneumonia according to age group[13].

DIAGNOSIS

Clinical diagnosis

There are no specific signs or symptoms of the disease. Signs most associated with PNM are fever (> 37.5oC), tachypnea, and signs of respiratory distress. Cough and fever are present in more than 80% of children analyzed in various studies[2]. Hypoxemia (< 97%) is also a clinical sign that should be valued, especially if associated with respiratory distress. Chest pain helps in diagnosis in adolescents. The absence of tachypnea has a greater value in ruling out PNM than the

Table 1. Main etiological agents of PNM according to age group.

Up to 2 months	B-group *Streptococcus*, enterobacteria, *Listeria monocytogenes*, *Chlamydia trachomatis*, *S. aureus*, virus
From 2 to 6 months	*C. trachomatis*, virus, *S. pneumoniae*, *S. aureus*, *B. pertussis*
From 6 months to 5 years	Virus, *S. pneumoniae*, *H. influenzae*, *S. aureus*, *M. pneumoniae*, *Mycobacterium tuberculosis*
Older than 5 years	*S. pneumoniae*, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *M. tuberculosis*

presence of this signal to confirm the diagnosis. Changes in auscultation have no important diagnostic value and their low reproducibility contributes to explaining their poor performance[2,7]. PNM can also manifest as abdominal pain[7].

Diagnostic Imaging

Chest X-ray

Several guidelines do not recommend routine chest radiography for the diagnosis of pneumonia in patients who are well enough to be treated on an outpatient basis. However, this is a frequently requested exam, as the clinical definition of PNM is nonspecific, and semiological findings are subjective[14,15].

Agreement on the interpretation of Artex is weak. There is no evidence that the test has an impact on clinical outcomes. Radiological findings are also not useful for differentiating bacterial from viral causes[14]. In its early phase, bacterial PNM may yield a normal Artex[7]. Indications for Artex include: hospitalization, failure of initial antibiotic treatment, suspected alternative diagnoses (tuberculosis, foreign body aspiration) or complications (such as empyema, abscess, and necrosis)[15].

Chest ultrasound

With reduced costs and greater availability of portable equipment, studies have pointed to ultrasound as a possible new diagnostic tool for pneumonia in children[3].

Evidence suggests that, if performed appropriately by trained physicians, ultrasound can detect consolidation and other features suggestive of PNM in children with chest X-ray accuracy. Despite being an exam that does not expose the child to radiation, there are still limitations in the validation of this test to confirm pneumonia, given the lack of standardization in the interpretation of ultrasound findings. Currently, the technical limitations of ultrasound do not yet enable it to completely replace chest radiography[1,3].

Pulmonary magnetic nuclear resonance (MRI)

Cross-sectional imaging, such as magnetic resonance imaging and computed tomography are important when better pulmonary evaluation is required in the case of severe pneumonia or complications. Because it is a non-radiation exam, MRI has proven to be an alternative in diagnostic aid.

Despite the limitation of signal intensity caused by low proton density in lung tissue and artifacts secondary to respiratory movements and heartbeat, new imaging techniques have been employed to reduce these interferences. Different pneumonia findings, such as poorly defined nodules, ground-glass opacity, and consolidations, can be easily detected and differentiated by MRI. In addition, complications such as pleural effusion, empyema and pulmonary abscess are also demonstrated. Currently, MRI should be considered as an alternative to computed tomography to evaluate pneumonia and its complications[1,16].

Laboratory Tests

There is no indication of complementary exams for outpatients[8].

In hospitalized patients, the recommendation for blood count collection is weak. If requested, it should be interpreted within the clinical context and other complementary examinations[9].

Some biomarkers have been studied to predict disease severity and to differentiate bacterial from viral agents. C-reactive protein and procalcitonin are higher in bacterial PNM. However, there is a large overlap of values, which reduces the diagnostic impact[1,12].

Microbiological investigation should be considered in patients admitted to an intensive care unit and in those with PNM complications. The tests that may be ordered are blood culture (low positivity), immunofluorescence or viral PCR, mycoplasma serology, pleural fluid analysis and sputum culture[9,10].

Invasive tests (such as bronchoalveolar lavage, lung biopsy, or alveolar puncture) should be reserved for severe cases that do not respond satisfactorily to antimicrobials despite appropriate treatment[4].

Treatment

In outpatients, the decision starts with whether or not to prescribe antibiotics. The American Society of Infectious Diseases states that most preschoolers have viral PNM and therefore should not receive antibiotics. The British Thoracic Society, on the other hand, states that every child diagnosed with PNM should receive antibiotics, since it is not possible to safely distinguish between viral and bacterial conditions[8,9].

If typical bacterial PNM is suspected, healthy infants, preschoolers, schoolchildren and adolescents with current vaccination should receive amoxicillin as their first choice. In treatment failure, azithromycin may be associated (Table 2).

If clinical picture compatible with atypical PNM, prescribe macrolide.

In the case of influenza, initiate oseltamivir, even without diagnostic confirmation (greater benefit if started with less than 48 hours of symptomatology.).

Intravenous antibiotics should be prescribed if the child does not tolerate the oral route or if absorption is impaired (vomiting), if there are signs of sepsis or complicated pneumonia.

Treatment can be changed to oral when the patient is getting better; there is no fever for 24-48h and no diarrhea or vomiting.

Treatment time is usually 7 to 14 days, depending on the severity. Complicated pneumonia may require 3-6 weeks of treatment.

Patients with saturation < 92% should receive supplemental oxygen.

In patients with dyspnea or signs of fatigue, tube diet should be indicated. If the patient is severely ill or vomiting, it is preferable to administer fluids intravenously.

Respiratory physiotherapy is not indicated.

If the patient does not progress well, review the dose of antibiotics, consider comorbidities (immunodeficiency, cystic fibrosis), consider complications of pneumonia (pleural effusion, necrotizing pneumonia, and abscess) and investigate additional or resistant germ[8-10,12,17].

Indication for hospitalization[4,8,9,18]

Factors to consider when making hospitalization decisions:

- Clinical signs of severity;
  - o O_2Sat < 92%; cyanosis
  - o FR > 50 mpm (infants > 70)
  - o Tachycardia disproportionate to fever
  - o Signs of respiratory distress
  - o Capillary Filling Time > 2s
  - o Difficulty feeding
  - o Moaning/apnea
  - o Toxic Appearance
  - o Dehydration
- Severity risk factors;
  - o Congenital Heart Disease
  - o Bronchopulmonary dysplasia
  - o Cystic fibrosis
  - o Bronchiectasis
  - o Immunodeficiency
- Pleural effusion;
- Age < 3-6 months;
- Eating difficulty/vomiting preventing oral treatment
- Ability of caregivers

Prevention

The 10-valent vaccine reduced the incidence, hospitalization and mortality of pneumococcal pneumonia in Brazil. This effect is seen not only in vaccinated children, but also in the general community, which can be explained by the reduction in population airway colonization[19,20].

H. influenzae, *B. pertussis*, influenza and measles vaccines also had a positive impact on the prevention of childhood pneumonia. Bacterial pneumonia is a common complication of measles (*S. pneumoniae* is the most commonly isolated agent) and it is a major cause of death from measles[15,21].

CONCLUSION

Pneumonia is a common disease in childhood. Although its prevalence has decreased in recent years due to the introduction of vaccines against *S. pneumoniae, H. influenzae* and *B. pertussis*, this pathology is still a major cause of morbidity and mortality in children older than 1 month of life. For most cases, the diagnosis is made through anamnesis and physical examination. Complementary examinations are reserved for severe cases, associated with complications or that do not have a good initial clinical response. Treatment is started empirically with amoxicillin for outpatients and penicillin or ampicillin for hospitalized patients, usually with good response to the proposed treatment, as pneumococcus is the main bacterial etiological agent. Patients with unfavorable evolution need hospitalization and further investigation, as well as reevaluation of the therapeutic scheme. In these cases, it is important to request laboratory tests (such as blood count and culture) and imaging, for a better evaluation of the clinical picture and its extension. Cultures may assist in the isolation of the etiological agent and guide antimicrobial treatment to ensure adequate coverage of the isolated germ.

Table 2. Suggested empirical antibiotic therapy according to age group. (Adapted from reference 10 and 17.).

Age	Hospitalized	Alternative	Outpatient
Neonate	Ampicillin + gentamycin	Azithromycin or clarithromycin (if suspecting infection by *C. trachomatis* or *B. pertussis*)	-
1 - 3 months	Ampicillin + gentamicin (in younger than 2 months)	Azitromicina or claritromicina (if suspecting infection by *C. trachomatis* or *B. pertussis*)	-
4 months - 5 years	Penicillin or ampicillin (add a macrolide if non-responsive)	Amoxicillin + clavulanic acid or cefuroxime	Amoxicillin
5 years - 15 years	Penicillin or ampicillin (add a macrolide if non-responsive)	Amoxicillin + clavulanic acid or cefuroxime	Amoxicillin
S. aureus	Oxacillin	Vancomycin or linezolid (if MRSA)	Cephalexin or clindamycin (if MRSA)

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