

Management of Community Acquired Pneumonia



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Pneumonia is a common illness which causes significant morbidity and mortality all over the world, despite the availability of better and more potent antibiotics and improvement in supportive care. The problem increases with discrepancy in management despite the availability of guidelines for management. Pneumonia is often misdiagnosed and is commonly treated inadequately or over treated with misuse of potent antibiotics. This along with the increasing contact with health services is leading to an increase in infection with multi drug resistant (MDR) organisms which are of major concern. It is also important to consider the prevalence of specific organisms at that point of time. This is brought into focus by the recent H1N1 pandemic. A large number of pneumonias may be of viral etiology during an influenza outbreak.

Assessment of Severity and Site of Care

The presentation of pneumonia can vary from a mild, self limiting illness to a severe, life threatening illness with significant mortality. Thus the most important decision facing the physician once a diagnosis of pneumonia is confirmed is the site of care. This decision affects both patient outcomes and healthcare costs. A careful assessment of the severity of illness at presentation is required to decide the site of care which could be outpatient, in a hospital ward or in an intensive care unit (ICU). Severity assessment also affects decisions regarding the extent of microbiological evaluation, the choice and route of administration of antibiotics and the level of supportive care. It has been seen that the admission rates vary significantly amongst physicians and the use of objective criteria for assessment of severity is essential for uniform and appropriate care. A decrease in mortality has been documented with the implementation of guidelines based management.^{1,2}

Several variables have been assessed as predictors of outcome and no single parameter has been found to accurately predict the severity of CAP. Several predictive models and scoring systems have been developed and validated to help develop uniform, guidelines based protocols. The two most important ones are the pneumonia severity index (PSI) and CURB65. Neither can unequivocally categorize patients and should be combined with clinical judgment.

PSI was developed in the United States as part of the Pneumonia Patient Outcomes Research Team (PORT) prospective cohort study for identifying patients with CAP at low risk for mortality.³ PSI stratifies patients into 5 risk classes on the basis of 20 variables. Class 1 and 2 patients can be treated as outpatients, class 3 need to be in an observation unit while class 4 and 5 should be treated as inpatients. PSI was developed to stratify patients into risk categories on the basis of short term mortality and this quantification is then linked to decisions regarding site and level of treatment. One major drawback with PSI is its complexity and the difficulty in calculating the score in the outpatient or emergency department.

CURB 65 is a simpler scoring system which is easier to remember and apply. It was developed on the basis of a prospective study on patients from United Kingdom, New Zealand and Netherlands.⁴ CURB65 uses five variables which include confusion, urea more than 20mg/dl, respiratory rate more than 30/min, blood pressure (systolic blood pressure less than 90 mm/hg or diastolic blood pressure less than 60 mm/hg) and age more than 65 years. Each parameter is assigned one point to get a severity score. The recommendations on the basis of CURB65 scoring are outpatient treatment for patients with a score of 0-1, hospital admission for a score of 2 and consideration for admission to ICU with a score of 3 or more. CRB 65 can be used when urea levels are not available. CRB65 has the benefit of using only clinical parameters and has been found to have discriminatory value similar to CURB65.⁵

Amongst the above PSI is probably a little better validated while CURB65 is much easier to apply and has similar discriminatory levels. Also PSI is more a predictor of mortality than a severity assessment score and this quantification is then used to decide the site of treatment, while CURB65 is a scoring for the severity of illness which makes site of treatment decisions easier. Various other severity scores or predictive models for decision regarding admission to ICU in CAP have been developed but PSI and CURB65 are the most validated. ATS guidelines⁶ have also laid stress on objective criteria to define the subset of patients who would benefit from ICU admission. These include the following major and minor criteria:

Major criteria:

1. Mechanical ventilation
2. Hypotension requiring vasopressors

Minor criteria:

1. Respiratory rate more than 30/min
2. Confusion or disorientation
3. Hypothermia
4. Hypotension requiring intravenous fluids
5. Leucopenia
6. Thrombocytopenia
7. Urea more than 20mg/dl
8. $\text{PaO}_2/\text{FiO}_2 \leq 250$

Any of the major criteria or three or more minor criteria are indication for ICU admission. All clinical prediction rules are supplements to clinical judgment which is of prime importance. A regular reassessment of disease severity is required after admission for further management related decisions. Assessment should be done at the time of presentation but it should also be dynamic and be done at regular intervals as stable patients may subsequently deteriorate and need admission or ICU care.

Treatment

Antimicrobial Therapy

The first step in treatment of CAP following severity assessment and decision regarding site of care, is initiation of treatment with appropriate antibiotics as bacteria are the most common pathogen. Early initiation of antibiotics is

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seen to abbreviate the illness and lead to a decrease in both complications and mortality. This is usually empirical as the organism is not isolated in a large proportion of patients at the onset. Also, the clinical and radiological picture is not a good predictor of the pathogen. The choice of appropriate antibiotic is further complicated by the emergence of MDR organisms in the community and is dependent on various parameters which include:

- The likely pathogen
- The resistance pattern in the community
- Risk of antibiotic resistance
- Severity of pneumonia
- Comorbid illnesses.

A wide variety of organisms can cause CAP but the likely pathogens according to the site of treatment categories are:⁷

- Outpatients –
 - Streptococcus pneumoniae
 - Mycoplasma pneumoniae
 - Haemophilus influenzae
 - Chlamydia pneumoniae
 - Respiratory viruses
- Inpatient(non ICU) –
 - Streptococcus pneumoniae
 - Mycoplasma pneumoniae
 - Chlamydia pneumoniae
 - Haemophilus influenzae
 - Legionella
 - Aspiration
 - Respiratory viruses
- Inpatient(ICU) –
 - Streptococcus pneumoniae
 - Staphylococcus aureus
 - Legionella
 - Gram negative bacilli
 - Haemophilus Influenzae

Ideally treatment for CAP should be detected by the organism identified by culture or serology and should be based on the sensitivity pattern. However, in a majority of patients, especially in our country, no definite organism can be identified due to a number of reasons and treatment is empirical based on surveillance data and “best guess” method. Therefore, the underlying background of the patient and the epidemiological surrounding should be considered while taking a decision regarding antibiotics. For example, in an alcoholic with CAP due to aspiration one should cover for anaerobic organisms.

The following considerations should be kept in mind while deciding on treatment options in CAP-

- Severity of illness
- Associated comorbid conditions like COPD, diabetes, etc
- Epidemiological background when the pneumonia occurs, like after a binge of alcohol, during an epidemic of influenza or in a nursing home resident.
- Possible resistance pattern that may be present due to various factors like chronic or recent antibiotic use.

Streptococcus pneumonia remains the commonest organism in all settings and drug resistant Streptococcus pneumoniae are being identified with increasing frequency. The risk factors for drug resistant Streptococcus pneumoniae infections include:

- Age more than 65 years
- Use of beta-lactams, macrolides, or fluoroquinolones within the past three to six months
- Alcoholism
- Medical comorbidities
- Immunosuppressed state

Certain risk factors predispose to infections by specific organisms and should be considered at the initiation of empirical therapy. These include:⁸

- Alcoholism
- Smoking or COPD
- Conditions predisposing to aspiration
- Lung abscess
- Structural lung disease
- Endobronchial obstruction
- Intravenous drug abuser
- HIV infection
- Exposure to zoonotic infections
- Travel to areas endemic for specific infections

Guidelines have been developed regarding the empirical initiation of appropriate antibiotics in accordance with the above factors. These should be followed in tandem with clinical judgment as inappropriate use of antibiotics leads to increase in cost of treatment, healthcare associated infections and emergence of multidrug resistant organisms. The most commonly followed guidelines are those from ATS⁹ and BTS¹⁰ guideline. In addition practice guidelines from PGIMER,¹¹ Chandigarh add an Indian perspective. A summary of the guidelines can be seen in the following table-

The Indian guidelines from PGIMER,¹⁰ Chandigarh do not recommend the use of tetracycline derivatives as monotherapy as most Streptococcus pneumoniae showed a high rate of resistance to the same. Also a need to limit the use of fluoroquinolones was stressed upon as it leads to a delay in the diagnosis of tuberculosis which is a common mimic of CAP in India. In addition fluoroquinolones lead to an increase in multidrug organisms resistant to both fluoroquinolones and other antibiotics and is also a strong risk factor for clostridium difficile diarrhea.

The BTS⁹ guidelines lays stress on amoxicillin as it is found to be effective against most strains of streptococcus pneumoniae with decreased sensitivity to penicillin in the recommended dose of 500 to 1000 mg thrice a day. Also streptococcus pneumoniae shows high level resistance to macrolides. In addition the BTS⁹ guidelines do not emphasize on covering atypical pathogens in the empirical therapy for patients treated as outpatients. This is explained by the fact that mycoplasma is the only atypical pathogen common in the community and it usually causes a mild, self limiting illness in young adults.

In our setting, the most appropriate treatment might be a beta lactam plus macrolide in the outpatient setting and an intravenous beta lactam plus a respiratory fluoroquinolone in the inpatient setting.

Intravenous antibiotics are indicated for hospitalized patients

Table 1 : Guideines for the management of pneumonia

	Outpatient	Inpatient (non-ICU)	Inpatient (ICU)
IDSA /ATS consensus guidelines (2007) ⁸	<ol style="list-style-type: none"> 1. Healthy with no use of antimicrobials in the previous 3 months: Macrolides or doxycycline 2. Comorbidities including chronic heart, lung, liver or renal disease; diabetes; alcoholism; malignancy; immunosuppressed state; use of antimicrobials in the previous 3 or in areas with high rate of infection with high level macrolide resistant Streptococcus pneumoniae: A respiratory fluoroquinolone or a beta lactam plus a macrolide 	<p>A respiratory fluoroquinolone or a beta lactam plus a macrolide</p>	<ol style="list-style-type: none"> 1. A beta lactam (cefotaxime, ceftriaxone or ampicillin-sulbactam) plus azithromycin/ a respiratory fluoroquinolone 2. If pseudomonas is suspected: An antipneumococcal, antipseudomonal beta lactam(piperacillin-tazobactam, cefepime, meropenem or imipenem) plus ciprofloxacin or levofloxacin or Above beta lactam plus aminoglycoside and azithromycin or Above beta lactam plus aminoglycoside and antipneumococcal fluoroquinolones 3. If MRSA is suspected: Add vancomycin or linezolid
BTS guidelines (October 2009) ⁹	Amoxicillin 500-1000mg thrice a day or clarithromycin/ erythromycin or doxycycline	<ol style="list-style-type: none"> 1. If oral therapy possible: Amoxicillin plus clarithromycin or Doxycycline or Levofloxacin or Moxifloxacin 2. If oral therapy not possible: IV amoxicillin or benzylpenicillin plus clarithromycin Or IV levofloxacin 	<p>Co-amoxiclav plus clarithromycin (plus levofloxacin if legionella is suspected) or Cefuroxime/cefotaxime/ ceftriaxone plus clarithromycin (plus levofloxacin if legionella is suspected) or Benzylpenicillin plus levofloxacin/ ciprofloxacin</p>
PGIMER, Chandigarh guidelines (2006) ¹⁰	<ol style="list-style-type: none"> 1. No comorbidities: Oral beta lactam or macrolide or fluoroquinolone 2. Coexisting medical comorbidities: Oral beta lactam plus macrolide/ doxycycline/ fluoroquinolone 	<p>Oral/IV beta lactam plus macrolide/ respiratory fluoroquinolone</p>	<p>IV beta lactam plus macrolide/ respiratory fluoroquinolone</p>

who are hemodynamically unstable, unable to take orally or have reasons to suspect impaired gastrointestinal absorption. They should be switched to oral therapy as soon as they are clinically stable, fully conscious, able to take orally and have a normally functioning gastrointestinal tract.

All patients who require hospitalization and patients who do not show clinical response at 48-72 hours should have investigations for identifying the causative organism and empirical antibiotics should be modified once the culture and sensitivity report is available.

Time of initiation and duration of antibiotics

Early administration of antibiotics is seen to decrease mortality in patients with confirmed diagnosis of CAP.¹² It is recommended that the diagnosis of CAP be confirmed with a chest radiograph and the first dose of antibiotic be subsequently administered within 4-6 hours. Outpatients should receive treatment with antibiotics for 5-7 days depending on clinical response.¹³ Clinical response is usually seen after 48 to 72 hours when a review is advisable. The patient should be afebrile and clinically stable for 48-72 hours prior to discontinuation of antibiotics. A shorter duration of treatment is advised for drugs like azithromycin which have a long half life.

Inpatients usually require antibiotics for 7-10 days, but treatment may be prolonged for 14-21 days depending on clinical assessment. A regular review of initial disease severity and clinical response is required.

Supportive management

Outpatients should be advised rest, adequate hydration, avoiding smoking and symptomatic treatment for fever, bodyaches and pleuritic chest pain.

Hospitalised patients should have regular monitoring of temperature, pulse, respiratory rate, blood pressure, oxygenation and mental status. Supportive management would include intravenous fluids, oxygen to maintain a $pO_2 > 60$ mm Hg or oxygen saturation above 94%, nutritional support, DVT prophylaxis if bedridden and ventilatory support. No major benefit is seen from NIV or CPAP and should only be tried in a setting with facilities for endotracheal intubation and mechanical ventilation.

Response to therapy and indication for discharge

Response is usually assessed clinically and is essential for decisions regarding duration of therapy, upgrading therapy, timing of discharge and to identify the group of non responders.

Clinical parameters used to assess clinical response are temperature <37.8 C, pulse <100/min, respiratory rate <24/min, systolic blood pressure >90 mm Hg, oxygen saturation >90% or pO₂ >60 mm Hg, ability to take orally and normal mental status. It has been seen that if one or more of these criteria are abnormal at the time of discharge, readmission and mortality within 6 months increases.¹⁴ Radiographic response lags behind clinical response and need not be assessed if the patient shows adequate clinical response. A repeat radiograph is required only if the patient deteriorates, does not respond, shows inadequate response or is at high risk for a cause of nonresolving pneumonia.

Non resolving pneumonia

There is no consensus on a definition for non resolving pneumonia which is based on clinical or radiological response and there is no definite guideline regarding the duration in which response should be seen. This term encompasses cases which progress or do not resolve completely despite appropriate therapy in an expected duration of time. Failure to show radiological response in 4-6 weeks has been considered a non responder and further evaluation for a cause is required. A more precise definition describes non resolving pneumonia as a pneumonia in which clinical features do not improve/worsen despite antibiotic therapy for 10 days or there is failure of radiological infiltrates to resolve in 12 weeks.¹⁵ Non resolving pneumonia is seen in 6-15%¹⁶ cases of hospitalized patients with CAP, while the incidence is not well known in the non hospitalized patients. A variety of causes can lead to non resolving pneumonia and these include causes related to the pathogen, host, complications and misdiagnosis of a noninfectious disease. The common causes are:

Pathogen related-

- Non bacterial pathogen like mycobacterium tuberculosis and atypical mycobacteria, fungi, nocardia and actinomycetes
- Organism not covered by the empirical antibiotics
- Resistant organism

Host related-

- Severity of initial illness
- Comorbidities
- Immunosuppressed state

Complications

- Parapneumonic effusion or empyema
- Abscess
- Metastatic infection
- Nosocomial superinfection

Non infectious diseases (wrong diagnosis)

- Neoplastic disorders
- Pulmonary embolism
- Systemic vasculitis including Wegener's granulomatosis and alveolar hemorrhagic disorders
- BOOP
- Eosinophilic pneumonias
- Congestive cardiac failure

Further evaluation in the form of microbiological tests for the etiological agent, CT Chest, bronchoscopy, biopsy and other tests specific to the suspected organism are required for these patients.

In conclusion CAP continues to be significant cause of

morbidity and mortality globally. Treatment in most cases continues to be empirical. Appropriate, guideline based evaluation and management of CAP can significantly reduce disease related morbidity and mortality along with a reduction in the emergence of MDR organisms. However, proper clinical evaluation including underlying illness, previous treatment and epidemiological background are important factors when deciding empirical antibiotic therapy in CAP.

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