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Management of Community Acquired Pneumonia

Ashutosh Nath Aggarwal and Ritesh Agarwal
Department of Pulmonary Medicine,
Postgraduate Institute of Medical Education and Research (PGIMER),
Chandigarh

Abstract

Appropriate antibiotic therapy remains the cornerstone of management of community acquired pneumonia (CAP). Even though this is mostly empiric, host, microbiological and epidemiological factors should be taken into account while deciding the antimicrobial agent(s) to be used. Available data from India suggests that the prevalence of drug resistant *Streptococcus pneumoniae* (DRSP) in the community is at present negligible and therefore treatment failure is unlikely to result if penicillin derivatives are used for treatment of CAP in previously healthy individuals with no risk factors for drug resistance. It is important to choose antibiotics judiciously in order to prevent the development of drug resistant strains. Irrational and unnecessary prescriptions especially those involving newer/ costlier antibiotics or their combinations should be avoided since these are not superior in efficacy. Some patients with CAP present on rapidly progress to acute hypoxemic respiratory failure (AHRF) and acute respiratory distress syndrome (ARDS) requiring mechanical ventilation (MV). Mortality in these patients can exceed 50% and hence they should be managed in an intensive care unit (ICU) setting. The mainstays of management of CAP associated with AHRF are oxygen therapy,

Correspondence: Dr. Ashutosh Nath Aggarwal M.D., D.M., Associate Professor, Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research (PGIMER), Sector 12, Chandigarh, India –160012. Phone: +91–172–2756824; Fax: +91–172–2748215. E-mail: ashutosh@indiachest.org

antibiotics and ventilatory support (when needed). Most patients with severe CAP and ARDS require invasive MV. The open lung approach should be used during MV.

Key Words: Community acquired pneumonia, antibiotic, acute respiratory distress syndrome, acute hypoxemic respiratory failure, mechanical ventilation

Introduction

The cornerstone of management of community acquired pneumonia (CAP) remains appropriate antibiotic therapy. However, treatment needs to be rational and evidence-based to prove beneficial to the patient, in particular, and the community, in general. Several clinicians tend to prescribe new and costlier antibiotics to these patients, with the hope that these will prove more efficacious. However, this generally is not always true. While it is proper to initiate treatment empirically once a patient presents with CAP, several epidemiological, patient, pathogen and drug related factors must be taken into account to tailor therapy to an individual patient's needs (Table 1).

Table 1 : Important considerations influencing antibiotic treatment in patients with community acquired pneumonia

- Spectrum of pathogens in local community
- Severity of disease
- Comorbidities and other risk factors
- Outpatient or inpatient or ICU management
- Route of administration
- Timing of initiation
- Duration of treatment
- Cost of drugs

Spectrum Of Pathogens

Data on microorganisms resulting in CAP is rather limited from India, and the reasons are not hard to fathom. Based on published reports and general clinical experience, it appears that *Streptococcus pneumoniae* is the commonest bacterial pathogen responsible for CAP in India, as elsewhere (1, 2). The data on atypical microorganisms causing CAP is even more sketchy from this country. Three reports from Delhi estimated the prevalence of Mycoplasma at about 30% in children and 35% in adults (3-5). Two reports from South India suggest estimates of 11% and 28% in adults (6, 7). Another study from Shimla reported Mycoplasma prevalence at 15% (2). The

prevalence of Chlamydia infection has been variably reported between 5.5% to 6.5% among children and adults with CAP (3, 8, 9). Since these studies are largely hospital-based, and have used different laboratory tests to identify presence of atypical microorganisms, it is not correct to extrapolate these data to the general population across the entire country. All one can infer from these results is that a significant proportion of CAP in India is likely to be caused by atypical pathogens, and therefore any treatment prescription should ideally ensure that these microorganisms are adequately covered.

Drug Resistance

Another important issue is that of CAP due to bacteria resistant of conventionally used antibiotics. There has been a recent global increase in the incidence of CAP related to beta-lactam resistant pneumococcal strains. It is generally believed that India shows a similar trend, and this has notably influenced prescription habits in the recent past. Unfortunately, this assumption is not fully backed by scientific evidence. In the recent Asian Network for Surveillance of Resistant Pathogens (ANSORP) study involving eleven Asian countries, 77 pneumococcal isolates from Vellore were evaluated (10). None of the isolates studied was beta-lactam resistant (defined as MIC exceeding 2.0 mg/mL), and only 7.8% isolates showed intermediate resistance (defined as MIC 0.12-2.0 mg/mL). In contrast, the Asian isolates together had an overall resistance of 25% and an intermediate resistance of 23% (10). This data suggests that beta-lactam resistance in pneumococcus is still not a significant problem in India. Similar results have earlier been published from Pondicherry, where only 7.3% intermediate resistance (and no resistance) was observed. Although the best treatment modality for resistant bacteria is still not clear, it can be concluded that the prevalent level and nature of drug resistance is unlikely to result in treatment failure if appropriate antibiotics in proper doses are chosen. In general, age more than 65 years, beta-lactam therapy in previous three months, medical comorbidities, alcoholism, and immunosuppressive states tend to increase risk of infection by beta-lactam resistant pneumococcus.

Inpatient Or Outpatient Treatment

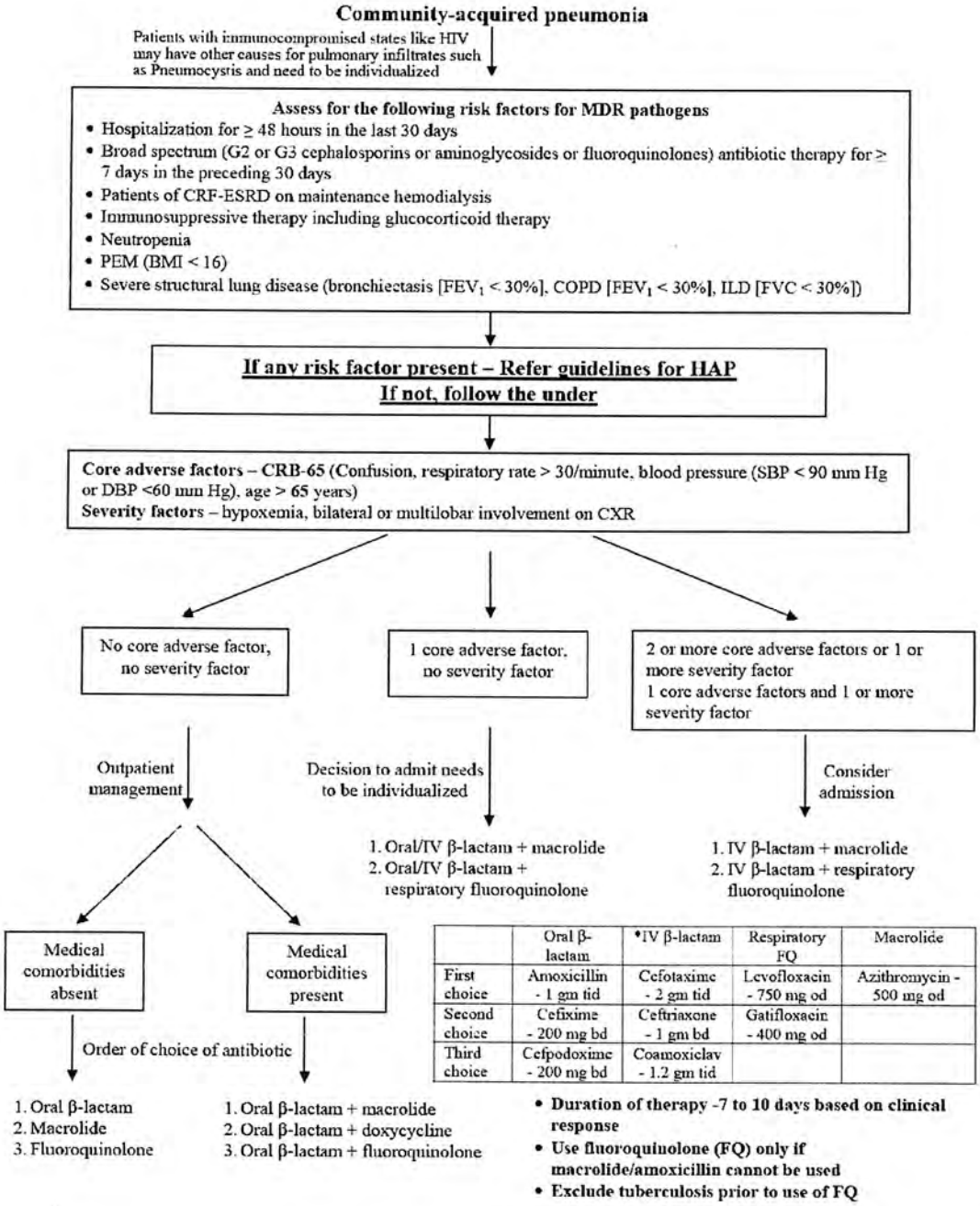
One of the most important decisions that ultimately guide antibiotic treatment is whether a patient with pneumonia needs therapy on outpatient or inpatient basis. Without doubt, the most important factor in this choice is the severity of pneumonia. However, other vital factors like presence of complications (such as lung abscess, empyema, meningitis, etc.), ability to take oral medications, and level of outpatient support

resources (such as family and social support, and distance of residence from health care service providers) are also central to this decision process.

There are several ways to assess disease severity. The judgment of treating physician is of course the most important. However, it remains largely subjective, and based on one's experience and clinical acumen. Physicians often tend to overestimate severity and hospitalize otherwise low-risk patients. It is therefore desirable that severity assessment in this fashion be supplemented by more objective and easily measurable parameters. Lately, several objective site-of-care scales have been developed for this purpose. Pneumonia Severity Index is a prognostic model developed from data on more than 14,000 patients, that classifies patients into five categories of increasing mortality risk (11). It has been suggested that Class I and II patients can be treated on outpatient basis, Class III patients should be placed in an observation unit, and Class IV and V patients should receive treatment as inpatient. However, calculation of this index is based on a large number of demographic features, patient history and examination, and laboratory variables. A much simpler score - CURB65 - takes into account only five variables (confusion, uremia, respiratory rate, low blood pressure, and age above 65 years) (12). Patient with none or one of these factors can be treated on outpatient basis, those with two factors need hospitalization, and patient with more factors often require ICU care. To make these criteria more suitable for primary level, it has also been suggested that of blood urea assessment can be altogether dropped (CRB65 score) (13) without compromising the value of the scoring system.

Empiric Choice Of Antibiotics

Antibiotic treatment for CAP is generally started empirically, as important time may be lost in submitting sputum samples for culture and awaiting microbiological results. The treatment generally aims at coverage of important pathogens (both typical and atypical) causing pneumonia in a particular group of patients. Elaborate guidelines exist to assist the clinician in selecting antibiotics suitable for a given patient. The most recent and widely followed among these were recently jointly issued by the Infectious Disease Society of America (IDSA) and American Thoracic Society (ATS) (14). However, these guidelines may not be truly applicable to Indian conditions due to differences in prevalence of pathogens, drug resistance patterns, and cost and availability of antibiotics. We had recently formulated guidelines on this issue for use in India (15). This algorithmic approach (Fig. 1) serves to emphasize important differences in



	Oral β-lactam	•IV β-lactam	Respiratory FQ	Macrolide
First choice	Amoxicillin - 1 gm tid	Cefotaxime - 2 gm tid	Levofloxacin - 750 mg od	Azithromycin - 500 mg od
Second choice	Cefixime - 200 mg bd	Ceftriaxone - 1 gm bd	Gatifloxacin - 400 mg od	
Third choice	Cefpodoxime - 200 mg bd	Coamoxiclav - 1.2 gm tid		

Figure 1: Algorithmic approach recommended for use in India for patient stratification and initial empiric antibiotic choice for patients with CAP

ideal treatment practices as appropriate to the Indian clinical setting.

The initial empiric choice of antibiotics is guided by several host and pathogen factors, since different antibiotics (and their combinations) may be more suitable for specific groups of patients. A brief summary of these guidelines is provided in Table 2. Certain notable differences between the IDSA/ATS recommendations and our institutional guidelines deserve special attention. For previously healthy

Table 2: Summary of options available for initial antibiotic therapy

Patient category and site of treatment	IDSA/ATS Guidelines[14]	PGIMER Guidelines[15]
Outpatient treatment for previously healthy patients with no risk factors for drug resistant *Streptococcus pneumoniae*	Macrolide (Azithromycin or Clarithromycin) *OR* Doxycycline	Beta-lactam (Amoxicillin or Cefpodoxime or Cefixime) *OR* Macrolide (Azithromycin)
Outpatient treatment for patients with comorbidities	Respiratory fluoroquinolone *OR* Beta-lactam plus Macrolide *OR* Beta-lactam plus Doxycycline	Beta-lactam plus Macrolide *OR* Beta-lactam plus Doxycycline *OR* Beta-lactam plus Respiratory fluoroquinolone
Inpatient (non-ICU) treatment	Respiratory fluoroquinolone *OR* Beta-lactam plus Macrolide	Beta-lactam plus Macrolide *OR* Beta-lactam plus Respiratory fluoroquinolone
ICU treatment [a,b]	Beta-lactam plus Macrolide *OR* Beta-lactam plus Respiratory fluoroquinolone	Beta-lactam plus Macrolide *OR* Beta-lactam plus Respiratory fluoroquinolone

[a] In patients where Pseudomonas infection may be a consideration, antipneumococcal antipseudomonal beta-lactam (piperacillin-tazobactam, cefepime, or imipenem), plus either a fluoroquinolone (ciprofloxacin or levofloxacin) or a combination of aminoglycoside plus azithromycin, may be preferred

[b] If methicillin-resistant *Staphylococcus aureus* (MRSA) is a consideration, add vancomycin or linezolid

individuals with no risk factors for drug resistance, it may be acceptable to use penicillin derivatives as the prevalence of penicillin-resistant pneumococcus appears negligible in the community at present. On the other hand, a high proportion of strains at our institute are innately resistant to tetracycline, and hence this group of drugs should be avoided. Tetracycline derivatives may, however, be used in combination with beta-lactam antibiotics in patients with comorbidities or other risk factors for drug resistance. The use of respiratory fluoroquinolones should also be discouraged in any setting with high tuberculosis prevalence. Since similar clinical and radiological findings may be present in pulmonary tuberculosis, inappropriate administration of fluoroquinolones that possess good antimycobacterial activity as well may lead to delay in diagnosis of tuberculosis in case it is the true diagnosis. Some other drugs recommended in the IDSA/ATS guidelines are either not currently freely available in Indian market or quite expensive for routine use.

While the initial treatment is empiric, it must be suitably modified if and when a microbiological diagnosis is achieved. Therapeutic options may be simplified, and the antibiotic spectrum must be appropriately narrowed based on drug sensitivity profile.

Time To First Antibiotic Dose

Two retrospective studies in USA have shown better survival among patients of CAP who received antibiotics early (16, 17). However, prospective studies have failed to show a similar improvement in either outcome or clinical stability (18-20). It is therefore difficult to recommend a specific window period within which antibiotics should preferably be started, although the general dictum, that treatment should be initiated as early as feasible after the diagnosis of CAP is considered likely, remains valid. For patients needing inpatient care, the initial dose may be instituted prior to hospitalization (for instance, the emergency services) (18).

Route Of Administration Of Antibiotics

Critically ill patients, those with severe disease, and those unable to swallow or tolerate oral medications are preferably treated with intravenous antibiotics. An attempt must be made to switch to oral therapy as early as possible. Generally this is feasible once the patient has shown clinical improvement, is hemodynamically

stable, can ingest oral drugs, and has a well functioning gastrointestinal tract (21). Nearly two-third patients meet these criteria within three days of initiating treatment. In general, the antibiotic being administered parenterally is preferred in its oral formulation. If this is not available, then an oral antibiotic from the same drug class should be given. Once an oral switch has been made, it may not be necessary to keep the patient in hospital for further management or observation.

Duration Of Treatment

In past, most patients of CAP received treatment for 7-10 days. However, shorter courses of antibiotics as associated with a similarly good outcome. Much of this data has been generated from studies on newer antibiotics having more favorable pharmacokinetic profiles (such as azithromycin and levofloxacin) (22,23). A five-day course of standard antibiotics should prove sufficient for most patients having CAP. A longer duration of therapy may be necessary if the initial antibiotic was not active against the identified microorganism, or if CAP gets complicated by extrapulmonary dissemination. Patient should be otherwise clinically stable and afebrile for atleast 48-72 hours before discontinuation of antibiotics.

Management of Respiratory Failure in CAP

About 20% of patients with CAP require hospital admission for respiratory failure. The incidence of the disease severity varies with age, being higher in very young children and elderly people (24). Of the 167 patients with CAP admitted in the Adult Respiratory Intensive Care Unit of this Institute, the mean age was 44 years (Table 3). About 58-87% of patients with CAP seen at PGIMER, Chandigarh presented with respiratory failure requiring mechanical ventilation. Mortality in these patients can exceed 50% (25). In a retrospective study at the Respiratory ICU of this institute, the overall mortality was 49% (95% CI, 36-63) in 49 of 201 patients admitted with severe CAP over 15 months (26). In another recent report from this institute, infective pneumonia accounted for about 61% of all patients with acute respiratory distress syndrome, 22% cases were due aspiration and rest were due to other etiologies like vasculitis, tuberculosis, fat embolism, drowning, paraquat poisoning, etc. (27).

The mainstays of management of CAP are oxygen therapy, antibiotics and ventilator support when needed.

Table 3 : Distribution characteristics of patients with CAP admitted in the Adult RICU at the PGIMER, Chandigarh.

Age (years)	44 (28-58)
Gender distribution	
• Males	94 (56.3%)
• Females	73 (43.7%)
Transfer to RICU from	
• Emergency	119 (71.2%)
• Ward	48 (28.8%)
Days in hospital before transfer to RICU	1 (0-2)
Duration of RICU stay (days)	5 (2-9)
Duration of hospital stay (days)	8 (3-14)
Mortality rate	68 (40.7%)

Values are expressed as Median (IQR) or Number (%)

Oxygen Therapy

High-flow oxygen therapy with Venturi-mask is of prime importance and the inspired oxygen concentration (FiO_2) should be adjusted depending on the severity of acute respiratory failure. The basic objective is to achieve a desirable arterial oxygen tension (PaO_2) of about 60 mmHg with the lowest possible FiO_2.

Ventilatory Support

Non Invasive Ventilation

Non invasive ventilation (NIV) is institution of mechanical ventilation without the use of an endotracheal airway. There are several studies for and against its use in management of acute respiratory failure (ARF) in CAP.

The proponents of use of NIV in pneumonia and acute respiratory distress syndrome (ARDS) hypothesize that inspiratory positive airway pressure increases the tidal volume, decreases the inspiratory workload, decreases dead space ventilation, and decreases rate-related intrinsic PEEP by decreasing RR. On the other hand expiratory positive airway pressure prevents microatelectasis by increasing FRC prevents recurrent alveolar derecruitment (atelectotrauma) acting akin to PEEP (28).

In a meta-analysis by Keenan *et al* on the role of NIV in pneumonia which included 8 trials (366 patients), there was 23% reduction in rate of endotracheal intubation (95% CI, 10-

35) and 17%; reduction in ICU mortality (95% CI, 8-26) (29). Among the studies (5 trials, 218 patients) which reported the data on hospital mortality, the analysis revealed that there was10% reduction in hospital mortality; 95% CI, -7 to 27. Among the 7 trials included in the analysis for evaluation of reduction in length of ICU stay it was shown that the use of NIV decreased ICU length of stay by 1.9 days; 95% CI, 1.0-2.9 (29).

Although the data is encouraging but in a recent meta-analysis by Agarwal *et al* it was demonstrated that NIV does not decrease the rate of endotracheal intubation or hospital mortality in patients with ARDS (28).

Currently it can only be said that the role of NIV in pneumonia with ARDS/ARF is at best controversial. It should be judiciously and vigilantly used in management of pneumonia and/ or ARDS with facilities for endotracheal intubation and mechanical ventilation being readily available.

Invasive Ventilation

Most patients with severe CAP/ ARF receive invasive ventilation (88% in BTS study). There are no controlled trials on MV in patients with pneumonia without ARDS (30). Most centres manage these patients with ARDSnet strategy (Table 4) (31).

Table 4: Components of ARDSnet strategy

Ventilation strategy	
Mode	Volume Assist-control
Initial tidal volume	5-8 mL/kg PBW
Respiratory frequency	10-35/minute
PEEP as per FiO_2 requirements	0.3-6; 0.4-8; 0.5-10; 0.6-12; 0.7-14; 0.8-16; 0.9-18; 1.0-20
I:E	1:1-1:3
Flow waveform	Descending ramp
Goals	
Plateau pressure	= 32 cm H_2O
PaO_2	55-80 mm Hg
pH	7.2-7.4
Weaning	
Mode (once PEEP < 8 & FiO_2 0.4)	Pressure-support

The ARDSnet strategy was proven to be most useful strategy for the management of ARDS. In the famous ARMA study, the in-hospital mortality rate was 39.8 percent in the group treated with traditional tidal volumes and 31.0 percent in the group treated with lower tidal volumes (P=0.007) (31). Thus, mortality was reduced by 22 percent in the group treated with lower tidal volumes, a finding of major importance. Also, there was significant reduction in ventilator free days, breathing without assistance and days without non pulmonary organ failure.

Conclusions

It is important to chose antibiotics judiciously for treatment of CAP, and avoid irrational or unnecessary prescriptions. Empiric antibiotic administration remains the mainstay of therapy, but should take into account host, microbiological and epidemiological factors. Newer or costlier antibiotics, or their combinations, may not be necessarily superior in efficacy. There is high incidence of mortality in patients with CAP who develop respiratory failure. These patients should be managed in an ICU setting. Use of NIPPV in a controlled setting may be beneficial in a select group but most patients will eventually require mechanical ventilation. Ventilation with "Open lung approach" (ARDSnet protocol) should be the standard of care as per the available evidence.

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