

Efficacy of empirical antibiotic prescription for the treatment of community acquired pneumonia

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Abstract

Background: Community acquired pneumonia (CAP) is a leading cause of morbidity and mortality in Bangladesh. There is difficulty in identification of the causative organism due to lack of facility of sputum culture and sensitivity test in many hospitals of Bangladesh. So targeted anti microbial therapy is not possible and empirical antibiotic prescription is done. The choice of empirical selection of antibiotic should be the best effective drug for the treatment of CAP.

Objective: To assess the efficacy of selected empirical antibiotic selection for the treatment of CAP.

Methods: This prospective observational study involves 82 patients with CAP admitted in medicine ward of Khulna medical college hospital, Khulna, Bangladesh. Patients were selected by inclusion and exclusion criteria. Diagnosis of CAP was confirmed by chest x-ray. Empirical selection of antibiotic was based on clinical experience. Most of the patients were treated with combined antibiotic except a few with monotherapy. Evaluation of the empirical choice of antibiotic was done by the outcome. Data of different parameter were recorded during study in preformed proforma. Statistical analysis was done by using SPSS.

Result: Out of 82 patients 62 (76%) were male and 20 (24%) were female. Mean age was 54.4 (\pm 9.6) years. Duration of antibiotic treatment was 7 days. No drug related adverse effect was observed. One patient developed paraneumonic effusion and none of the patient developed lung parenchymal damage or lung abscess. All the patient recovered completely.

Conclusion: CAP is treated in many hospitals of Bangladesh by selecting the antibiotic empirically. Improvement of hospital laboratories to perform sputum for culture and sensitivity test is necessary for selecting an effective antibiotic.

Key words: Community acquired pneumonia, Empirical, Antibiotic.

Introduction

Community acquired pneumonia (CAP) is the pneumonia occurring outside the hospital or in long term care facility. It causes morbidity and mortality world wide. Adverse cardiovascular events can also occur. Patients present with cough, fever, chills, rigor, fatigue, dyspnoea and pleuritic chest pain. Assessment for the need of hospitalization is done by using the pneumonia severity index, CURB 65 score system combined with clinical judgment. CURB 65 scoring is done by calculating scores on Confusion (mini mental

state score <8), blood Urea level (> 7mmol/l), Respiratory rate (> 30/minute), Blood pressure (systolic blood pressure <90 mmHg and diastolic blood pressure < 60 mmHg) and Age > 65 years. One point score for each character and total point score is 5. Patient having score 0-1 is recommended for outpatient care, score 2 is recommended for in patient ward care and score 3 is recommended for in patient intensive care unit (ICU) care. Incidence of hospitalization is high among elderly adults.¹ Diagnosis is done by history, clinical features and by some

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investigations such as chest x ray, complete blood count, blood sugar, blood for culture and sensitivity test and sputum for culture and sensitivity (sputum for c/s) test.² Despite advanced diagnostic tests no organism can be detected in some cases and respiratory viruses are detected in few cases.³

Empirical selection of antimicrobial for the treatment is the cornerstone of management. To reduce the misuse of antibiotic and to avoid the antibiotic resistance an effective antibiotic selection is essential. Empirical selection means choice originating in or based on clinical experience. Follow up after the start of antibiotic is important.⁴ Empirical dual antibiotic therapy consisting of Beta-lactum plus macrolide (clarithromycin) or fluoroquinolone (levofloxacin) or doxycycline initiated within 4 to 8 hours of hospitalization was associated with lower mortality.^{5,6} Switch over from parenteral antibiotic to oral antibiotic can be done after improvement of symptoms when patient is afebrile and able to tolerate oral medication.⁷

CAP in out patient department can be treated with monotherapy using macrolide (clarithromycin) or doxycycline.⁸ Patients having co-morbidity like chronic obstructive pulmonary disease (COPD) can be treated with respiratory fluoroquinolone (levofloxacin or gemifloxacin or moxifloxacin) or an oral Beta-lactum plus a macrolide (clarithromycin) by empirical selection. Severe CAP admitted in ICU can be treated with a Beta-lactum plus a macrolide (azithromycin) or a respiratory fluoroquinolone. Patients with the risk of having pseudomonas infection can be treated with lactum antibiotic (such as piperacillin / tozabactam, imipenem / cilastatin, meropenem, doripenem or cefepime) plus an aminoglycoside or an anti pseudomonal fluoroquinolone (levofloxacin or ciprofloxacin). Those with the risk of methicillin resistant staphylococcus aureus infection can be treated with vancomycin or linezolid.^{9,10} Anti pneumococcal or anti influenza vaccination can be done in elderly patients to prevent CAP by these organisms.¹¹

The aim of this study was to emphasize on the choice of the empirical selection of antimicrobial. The choice should be the best possible drug for the treatment of CAP and individualized for each patient in terms of efficacy of the the antibiotic either as single agent or in combination treatment.

Materials and Methods

This prospective observational study was carried out in the medicine ward of Khulna medical college hospital, Khulna, Bangladesh, during a period of 6 months from 1st August 2018 to 31st January 2019. Ethical clearance was taken from the Ethical review committee of Khulna medical college, Khulna. Total 82 adult male and female patients with community acquired pneumonia (CAP) were enrolled in this study. Patients were selected by inclusion and exclusion criteria. Patients with pneumonia occurring outside the hospital were included in this study. Patients with pulmonary tuberculosis, pleural effusion due to tuberculosis, bronchogenic carcinoma, heart failure, renal failure and pregnant patients were not included in this study. Informed written consent was taken from each patient before their enrollment. History and physical examination was completed in each patient. CAP was defined as the presence of acute illness with two or more of the symptoms and signs of lower respiratory tract infection such as fever, cough, sputum, dyspnoea, chest pain, features of consolidation on examination of chest and presence of radiological features of consolidation in chest x ray. CAP severity index CURB 65 scoring was done by calculating scores on Confusion (mini mental state score < 8) blood Urea level (> 7mmol/l), Respiratory rate (> 30/minute), Blood pressure (systolic blood pressure < 90 mmHg and diastolic blood pressure < 60 mmHg) and Age > 65 years. One point score for each character and total point score is 5. Patient having score 0-1 is recommended for out patient care, score 2 is recommended for in-patient ward care and score 3 is recommended for in patient intensive care unit (ICU) care. Pulse, temperature and chest x-ray findings were recorded in each patient. Presence of co-morbid conditions such as asthma, chronic obstructive pulmonary disease (COPD), hypertension, diabetes mellitus, use of steroid or other immunosuppressive drugs and smoking habit were determined and recorded from history and treatment documents. Sputum character whether rusty or purulent was observed and recorded. Sputum culture and sensitivity test was not done due to lack of facility. Antibiotic was selected for each patient on empirical basis from the knowledge of previous experience and observation in treating the CAP patients. Antibiotics used were inj. Ceftriaxone 2gm iv daily in 12 (15%) patients. inj. Ceftriaxone 2 gm iv daily plus oral Clarithromycin 250 mg 12 hourly in 44

(55%) patients, oral Co-amoxiclav 375mg 8 hourly plus oral Clarithromycin 250 mg 12 hourly in 12 (15%) patients, inj. Ceftriaxone, 2 gm iv daily plus oral Cloxacillin 500 mg 6 hourly in 10 (12%) patients, inj. Ceftriaxone 2 gm iv daily plus oral Linezolid 600 mg 12 hourly in 2 (2%) patients and inj. Meropenem 500 mg iv 8 hourly in 2 (2%) patients. Antibiotic treatment was continued for 7 days. No drug related adverse effect was observed in any patient. Treatment outcome was observed and recorded by follow up of the clinical features and chest x ray findings done after 7 days. Chest x ray after 7 days reveals complete resolution of the lung consolidation. There was no lung parenchymal damage or abscess formation. Evaluation of the empirical use of antibiotic in individual patient was done by the outcome. Data of different parameter were recorded during study in preformed proforma. Statistical analysis was done by using SPSS.

Result

82 patients were enrolled in this study. 62 (76%) were male and 20 (24%) were female. Age was from 21 to 82 years. Mean age was 54.4 ± 9.6 years. Highest number of patients-20 (25%) were in 31 to 40 years age group and 22 (27%) patients were of > 65 years old. (Table-I)

Table I
Age and sex distribution of the patients

Age group in years	Number		Total	Mean age %
	Male	Female		
21-30	6	2	8	9
31-40	20	0	20	25
41-50	8	8	16	20
51-60	6	2	8	9
61-70	10	2	12	15
71-80	10	6	16	20
81-90	2	0	2	2
Total	62	20	82	100

28 (34%) patients were without any co-morbidities 54(66%) patients had co-morbidities such as diabetes mellitus (8-10%), immunosuppression due to steroid intake (4-4%), COPD (6-7%), asthma (8-10%), Parapneumonic effusion (1-1%), smoking habit (15-19%) and hypertension (12 - 15%) (Table-II).

Table II
Co-morbidities of the patients

Co-morbidity	No	%
Chronic obstructive pulmonary disease	6	7
Asthma	8	10
Smoking	15	19
Diabetes mellitus	8	10
Immunosuppression	4	4
Hypertension	12	15
Parapneumonic effusion	1	1
No Co-morbidity	28	34
Total	82	100

Highest number of patients 44 (55%) received dual therapy with inj. Ceftriaxone plus oral Clarithromycin. Dual therapy with oral Co-amoxiclav plus oral Clarithromycin was used in 12(15%) patients. Inj. Ceftriaxone plus Cloxacillin was used in 10 (12%) and inj Ceftriaxone plus oral Linezolid was used in 2(2%) patients. Monotherapy with inj Ceftriaxone was used in 12 (15%) and inj meropenem was used in 2 (2%) of patients. (Table-III)

Table III
Empirical selection of antibiotic

Antibiotic	Patient		Outcome	
	No	%	Recovery	Death
Inj. Ceftriaxone	12	15	12	0
Inj. Ceftriaxone plus oral Clarithromycin	44	55	44	0
Oral co-amoxiclav plus oral Clarithromycin	12	15	12	0
Inj. Ceftriaxone plus oral Cloxacillin	10	12	10	0
Inj. Ceftriaxone plus oral Linezolid	2	2	2	0
Inj. Meropenem	2	2	2	0
Total	82	100	82	00

Monotherapy with single antibiotic was used in 14 (18%) patients, dual therapy with two anti biotic was used in 56 (68%) patients. Triple antibiotic was used in 12 (14%) patients. (Table-IV)

Table IV
Number of antibiotic used for each patient

Number of antibiotic used	Patient	
	No	%
Mono therapy	14	18
Dual therapy	56	68
Triple therapy	12	14
Total	82	100

All the patients including patient with parapneumonic effusion recovered completely.¹ None of the patients developed lung parenchymal damage or lung abscess. No drug related adverse effects were observed in any patient.

Discussion

In Bangladesh there is lack of facility of sputum for culture and sensitivity (c/s) test even in teaching hospitals. So CAP is treated by antibiotic selected empirically from the knowledge of experience. In this study we observed the prescription pattern of antibiotic selected on empirical basis in the management of community acquired pneumonia. We evaluated the effectiveness of the antibiotic by monitoring the outcome of treatment. We have gone through a study carried out in medicine ward and pulmonology ward of Bangladesh institute of research and rehabilitation in diabetes, endocrine and metabolic disorders (BIRDEM) in Bangladesh and found that sputum for c/s test of CAP patient revealed the organism streptococcus pneumoniae, streptococcus pyogens, staphylococcus aureus, klebsiella pneumoniae. These organisms were sensitive to Ceftriaxone, Meropenem, Co amoxiclav, Clarithromycin and Linezolid.¹²

In a study from China common empirical antibiotic for CAP was monotherapy with Levofloxacin (15%).¹³ So there is geographical variation of micro organisms and antibiotic use for CAP treatment. In an American study it is observed that anti biotic treatment for CAP is started by empirical selection and thereafter adjustment of the anti biotic according to the sputum c/s test report is done. They recommended monotherapy with Macrolides or Doxycycline in most patients and Levofloxacin or Moxifloxacin as second line drug. Recommendations for the choice of antibiotic differ among guidelines and among the various subclasses of patients as in out patient care. In patient ward and in ICU patient, superiority of beta lactam and combination of beta lactam plus macrolide is based on cohort studies and observational studies.

Randomized controlled trial evaluates the efficacy of beta lactam antibiotic alone versus beta lactam plus macrolide or versus levofloxacin alone in the treatment of hospitalized CAP. Result showed the superiority of beta lactam in patients having CURB 65 score 0-1 and 2. Study describes the superiority of combination drug treatment with beta lactum plus macrolide in patients with more severe form of community acquired pneumonia having CURB 65 score>3.¹⁴

So empirical antibiotic selection is important for the effective management of CAP in resource poor hospital settings. We used monotherapy in 14 (18%) of cases. Dual therapy was used in most of the cases 56 (68%) and triple antibiotic was used in 12 (14%) patients. Multiple antibiotic was used because of inability to identify the organism causing CAP.

There are limitations of this study as it enrolled a small number of patients and it was a single centre study. Intensive care unit (ICU) patients with severe CAP were not included in this study. Multi centre study with large number of patients including ICU patients will reveal a better interpretation regarding the outcome of empirical selection of antibiotic in CAP patients.

Conclusion

CAP is treated in most of the hospitals, even in large teaching hospitals in Bangladesh by selecting the antibiotic empirically from the previous knowledge and experience of physicians in this geographical area. Although the outcome is good all these attempt can give rise to the development of antibiotic resistance and there is also misuse of antibiotic. So the improvement of hospital laboratories to perform sputum for culture and sensitivily test is necessary.

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