

Sputum Bacteriology and Antibiotic Sensitivity Pattern of Patients Having Acute Exacerbation of COPD in India – A Preliminary Study

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a common disease and equally affecting rural population. Majority of COPD exacerbations are infective and facilities of bacterial culture are not available at peripheral health institutions. Acute exacerbations can contribute to irreversible progression of disease.

Objective: To find out the bacteria predominantly causing the AECOPD in our region, its relation with severity of the diseases and antibiotic most effective against these organisms.

Material and Methods: Previously diagnosed patients presented with acute exacerbation were investigated for sputum characteristics, culture and drug sensitivity.

Results: Culture was positive in 41 (82%) patients. Streptococcus pneumoniae (32%) was the most common pathogen isolated followed by Streptococcus pyogenes (16%) and Pseudomonas (12%). Piperacillin+tazobactam was the most effective antibiotic against all organisms. Quinolones were less effective.

Discussion: Sputum culture was positive in 82% of patients with AECOPD which was higher as compare to other studies. On the contrary positive growth in 97% of samples has also been found. This difference may be because of the fact that culture positivity depends on nature of sputum, time of collection sputum and previous antibiotic use.

Conclusion: Streptococcus pneumoniae is still the most common pathogen in patients with AECOPD of this area. Piperacillin+tazobactam should be the first choice empirical antibiotic. Quinolones should be used cautiously in area where prevalence of tuberculosis is high. However more studies with larger population required which also includes bronchoscopic sampling along with sputum.

Keywords: Sputum; Bacteriology; Antibiogram; Acute exacerbation; Chronic obstructive pulmonary disease

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases [1]. COPD is the fourth leading cause of death in the world and will become the third leading cause of death worldwide by 2020 [1]. Four to ten percent adult male population of India and 3.5 to 6.5% population in Asia Pacific countries suffer from this disease [2].

An exacerbation of COPD is an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication [1]. Acute exacerbations forms the major component of economical burden of COPD [3]. AECOPD also leads to indirect costs because of days lost from work [4]. It is the important factor of mortality in COPD patients. AECOPD cause great impact on individual health and health care system in India also [2]. Acute exacerbations can contribute to irreversible progression of disease [5]. Therefore timely institution of correct management is imperative for better prognosis of disease. Bacterial infections are the most common cause of AECOPD [1]. It is estimated that bacterial infections are responsible for more than 40% of all exacerbations in India [6]. It has been found that use of antibiotics as well as type of antibiotics used to treat AECOPD has an impact on the failure rate [7]. Proper selection of antibiotic selection needs culture studies but it is time consuming and not available in majority of peripheral health institutions. Bacterial flora of AECOPD is changing from usual pathogen [8]. The choice of the antibiotic should be based on the local bacterial resistance pattern [1]. Therefore the knowledge

of bacterial flora of patients of AECOPD of that geographical area is required [9].

Facilities of bacterial culture are not available at majority of peripheral health institutions. There is no such study has been carried out in this part of country (Gujarat) and very limited data is available from India. Knowledge of local bacterial etiology and antibiotic sensitivity patterns of AECOPD facilitates early introduction of proper empirical antibiotics which can reduce the morbidity, mortality and improve prognosis particularly at peripheral level where facility for culture studies are not available. Current data on bacteriology related to AECOPD are mainly derived from the western countries. There are very limited data available in this aspect from Asia Pacific region.

So, we conducted this study to know the bacteria predominantly causing the AECOPD in our region and the antibiotic sensitivity pattern of these organism so that we can design a proper antibiotic regimen which will have a beneficial effect on the morbidity and mortality of the disease.

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Materials and Methods

The present prospective observational study was carried out at Dhiraj General Hospital, Piparia, Vadodara, Gujarat from March 2011 to June 2012 after taking institutional ethical committee permission with the following inclusion and exclusion criteria.

Inclusion criteria

Previously diagnosed patients of COPD on the basis of history of exposure to risk factors, clinical history and examination supported by spirometry having acute exacerbation according to the following criteria.

- Increased dyspnoea
- Increased sputum volume
- Increased sputum purulence
- Sputum sample contains <10 squamous epithelial cells and >25 pus cells

Exclusion criteria

Patients having bronchiectasis, tuberculosis, pneumonia, malignancy and other evident disease on chest x-ray

- Patients previously admitted within 21 days and taken antibiotics
- Patients having sputum positive for acid fast bacilli (AFB)

After clinical examination, routine CBC, blood sugar, urine examination, X-ray chest PA view, oxygen saturation by pulse oximetry, were done in all the patients. Their early morning sputum was collected in a sterile transparent container after rinsing the mouth with antiseptic solution. The sputum sample was examined for physical appearance, gram stain, AFB smear, pyogenic culture and drug sensitivity for bacteria.

Results

Total 50 patients were enrolled in the present study comprised of 41 males and nine females having mean age of 60.18 years. All males were smokers while all females though non-smokers, but exposed to biomass fuel. Sputum culture was positive for microbes in 82% of the patients. It can be seen from Table 1 that out of positive cultures *streptococcus pneumonia* (39%) and *streptococcus pyogenes* (19.5%) were most common pathogens followed by *pseudomonas aeruginosa* (14.7%), *klebsiella pneumonia* (9.7%), *H. influenza* (7.32%), *staphylococcus aureus* (4.88%) and *E. coli* (4.88%).

We had observed that out of all six patients with positive culture for *pseudomonas aeruginosa*, two (33.33%) had yellow green while four (66.67%) had green sputum. Out of remaining 44 patients 29 (65.91%) had white sputum and 15 (34.09%) had yellow sputum. All patients with yellow sputum had positive culture for pathogens while out of 29 patients having white sputum 20 (68.97%) patients had positive culture for pathogens. All nine patients in whom no pathogen was grown had white sputum. It can be seen from Table 1 that *pseudomonas aeruginosa* was more common in patients with FEV1<50% of the predicted value however no correlation was found between other organism with lung function.

Antibiotic sensitivity pattern to all organisms is shown in Table 2. Sensitivity of piperacilline+tazobactum and ofloxacin was tested in all 41 patients while of ciprofloxacin was tested in almost all (40) patients having positive culture for organism irrespective of gram positive or negative. It was found that piperacilline+tazobactum was the most effective antibiotic being sensitive to majority of organisms (95.12%).

In only two patients (one had positive culture for *streptococcus pneumonia* and one had *staphylococcus aureus*) it was found to be resistant while all gram negative organisms were sensitive. Quinolones were less effective being overall resistant of 39.02% with ofloxacin and 37.5% with ciprofloxacin. Levofloxacin was also resistant to 33.33% of patients having gram negative organisms. Co-amoxycylav was resistant to 34.62% and amoxycilline was resistant to 46.15% of the patients having gram positive organisms. Among macrolides, azithromycin was the most effective drug against gram positive organisms having resistance of 26.92% while erythromycin was the least effective drug having resistance of 69.23%. Linezolid was tested in 17 patients having gram positive organism and found to be resistant in 41.18%. Against gram negative organisms; apart from piperacilline+tazobactum, cefoperazone+sulbactam was also 100% effective while amikacin was sensitive in 92.86%. For most common organisms (*streptococcus pneumonia* and *streptococcus pyogenes*), piperacilline+tazobactum was most effective antibiotic in our region having sensitivity of 95.83%.

Discussion

COPD is leading cause of morbidity and mortality and early introduction of empirical antibiotics, can improve outcome and reduce mortality.8 Since culture facilities are not readily available and time consuming, it is better to know the pattern of bacterial flora and their sensitivity of a particular geographical area. Sputum culture was positive in 82% of patients with AECOPD which was higher as compare to other studies [6,10,11] This difference may be because of the fact that culture positivity depends on nature of sputum, time of collection sputum and previous antibiotic use. Madhavi et al. [11] have collected repeat samples if first sample were unsuitable after admission which can decrease yield particularly if empirical antibiotics has been started. Sputum collection timing has not been mentioned by Chawla et al. [6], which can affect yield as early morning sample may increase the yield as compared to randomly collected samples. Study by Ko et al. [10] was retrospective and time of collection of sputum has not been mentioned which can decrease yield. On the contrary other author [12] had found positive growth in 85 (97%) of the 88 representative samples.

In our study *Streptococcus pneumoniae* (32%) was still the most common pathogen in AECOPD in this area. This finding is contrary to other studies reported from India by Chawla et al. [6] who had found *Pseudomonas aeruginosa* while Madhavi et al. [11] had found *Klebsiella pneumonia* was the most common organism. The difference may be because most of the cases in our study were from rural area. Further, they had included more severe patients in their study. We also found *pseudomonas aeruginosa* was most common in patients having FEV1 <50% of predicted value in our study. Few authors [12-14] have found higher incidence of *pseudomonas* and *enterobacteriaceae* in patients with more severely compromised lung functions. Groenewegan et al.

Pathogen	Severity				Total
	Mild	Moderate	Severe	Very Severe	
No Organism	3	3	1	2	9
Streptococcus Pneumoniae	0	4	8	4	16
Streptococcus pyogenes	0	2	5	1	8
Staphylococcus aureus	0	2	0	0	2
Pseudomonas aeruginosa	0	1	2	3	6
Klebsiella Pneumoniae	0	2	0	2	4
H.influenzae	0	3	0	0	3
E. coli	0	1	0	1	2
Total	3	18	16	13	50

Table 1: Co-relation between severity of Chronic Obstructive Pulmonary Disease (COPD) and pathogens isolated from sputum.

	n	S. pneumonia (N=16)			S. pyogens (N=8)			P. aeruginosa (N=6)			K. pneumonia (N=4)			E. coli (N=2)			Staph. Aureus (N=2)			H. influenza (N=3)			Total		
		S	M	R	S	M	R	S	M	R	S	M	R	S	M	R	S	M	R	S	M	R	S	M	R
Piperacillin + tazobactam	41	15	0	1	7	1	0	6	0	0	4	0	0	2	0	0	1	0	1	3	0	0	38	1	2
Amoxycillin	29	7	2	7	4	1	3	0	0	0	0	0	0	0	0	0	0	0	2	2	0	1	13	3	13
Co-amoxycylav	29	9	3	4	3	1	4	0	0	0	0	0	0	0	0	0	1	0	1	3	0	0	16	4	9
Amikacin	14	0	0	0	0	0	0	5	0	0	3	0	1	2	0	0	0	0	0	3	0	0	13	0	1
Gentamicin	15	0	0	0	0	0	0	3	2	1	2	2	0	1	0	1	0	0	0	0	1	2	6	5	4
Tobramicin	15	0	0	0	0	0	0	4	1	1	2	0	2	1	1	0	0	0	0	2	1	0	9	3	3
Ciprofloxacin	40	9	0	6	5	0	3	3	0	3	4	0	0	1	0	1	0	0	2	2	1	0	24	1	15
Levofloxacin	15	0	0	0	0	0	0	3	0	3	4	0	0	1	0	1	0	0	0	2	0	1	10	0	5
Ofloxacin	41	7	2	7	5	0	3	3	0	3	3	1	0	1	0	1	0	0	2	2	1	0	21	4	16
Norfloracin	13	0	0	1	0	0	0	3	0	3	4	0	0	1	0	1	0	0	0	0	0	0	8	0	5
Azithromycin	29	10	1	5	5	2	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	17	4	8
Roxithromycin	21	6	0	2	3	0	5	0	0	0	0	0	0	0	0	0	0	0	2	0	1	2	9	1	11
Clarithromycin	21	4	2	2	3	0	5	0	0	0	0	0	0	0	0	0	0	0	2	0	1	2	7	3	11
Erythromycin	29	4	1	11	3	0	5	0	0	0	0	0	0	0	0	0	0	0	2	0	0	3	7	1	21
Vancomycin	20	5	0	4	1	0	5	0	0	0	0	0	0	0	0	0	1	1	0	0	0	3	7	1	12
Clindamicin	20	5	0	4	2	0	4	0	0	0	0	0	0	0	0	0	0	0	2	0	0	3	7	0	13
Linezolid	20	7	1	1	2	0	4	0	0	0	0	0	0	0	0	0	0	0	2	0	0	3	9	1	10
Imipenem	14	0	0	0	0	0	0	2	0	3	4	0	0	2	0	0	0	0	0	2	1	0	10	1	3
Meropenem + cilastatin	15	0	0	0	0	0	0	6	0	0	4	0	0	2	0	0	0	0	0	3	0	0	15	0	0
Ceftriaxone	15	0	0	0	0	0	0	3	0	3	3	0	1	1	0	1	0	0	0	3	0	0	10	0	5
Cefixime	15	0	0	0	0	0	0	1	0	5	1	0	3	0	0	2	0	0	0	0	1	2	2	1	12
Cefoperazone + sulbactam	15	0	0	0	0	0	0	6	0	0	4	0	0	2	0	0	0	0	0	2	1	0	14	1	0
Cefotaxime	15	0	0	0	0	0	0	3	0	3	3	0	1	1	0	1	0	0	0	2	1	0	9	1	5
Cefadroxil	20	6	0	2	3	0	4	0	0	0	0	0	0	0	0	0	0	0	2	0	1	2	9	1	10
Cefpodoxime	16	0	0	1	0	0	0	0	0	6	1	0	3	0	0	2	0	0	0	2	1	0	3	1	12
Cefuroxime	37	7	1	6	3	0	4	1	0	5	1	2	1	0	1	1	0	0	1	0	1	2	12	5	20

Table 2: Drug sensitivity pattern of various pathogens isolated from sputum (n=total number of patients tested, S=sensitive, M=moderately sensitive, R=resistant).

[12] had also included more severe patients but found hemophilus influenza (45%) as most frequent organism followed by *streptococcus pneumonia* (27%). However data on relationship between organism and lung function is scarce, it needs more studies with large number of patients.

We found that the piperacilline+tazobactam was the most effective organism in this area against all organism (gram positive and gram negative). But unfortunately studies [6,11] from other part of this country had not included this antibiotic in drug sensitivity test. They had found gram negative organisms most commonly in their study and quinolones was the most effective antibiotic against gram negative organisms. But we found quinolone to be less effective against gram negative organism. Ofloxacin was resistant in 26.67% and levofloxacin was resistant to 33.33% of patients having gram negative organisms. This may be because of very frequent use of quinolones in this area. Even though quinolones are effective, it should not be used frequently in our country where prevalence of tuberculosis is high.

Conclusion

Streptococcus pneumoniae is still the most common pathogen in patients with AECOPD of this area and piperacilline+tazobactam is the most effective antibiotic against all organisms. So, piperacilline+tazobactam should be the first choice empirical antibiotics for AECOPD patients in this area. Quinolones should be used cautiously in area where prevalence of tuberculosis is high.

Limitations

Spontaneously expectorated sputum was used for microbiological

sampling. The accuracy could be increased by taking sample bronchoscopically.

Recommendations

Large study is which include of all severity of the stable COPD patients as well as AECOPD patients with comparison of sputum (including quality) and bronchocopic sample cultures is required.

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