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Spectrum of Bacterial Pathogens and Their Antibiotics Sensitivity Patterns in the Sputum of Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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ABSTRACT

Aim-The aim of our study is to isolate bacterial pathogens in sputum culture of patients with acute exacerbation of COPD and sensitivity pattern of these pathogens.

Materials and Methods-The sample includes a total of 60 AECOPD patients with positive sputum culture was taken in to the study after satisfying all the criteria.Two sputum samples were collected from each patient, one at the time of admission and the other early in the morning. Routine hematological investigations and chest x-ray were done on the day of presentation. The data was entered into Microsoft excel spreadsheet 2007 and analysed using IBM SPSS Version 16.0. Basic descriptive statistics were used to summarise the data.

Results-The age group of the patients studied ranged from 45 to 82 years, the most common age group being 56 to 65 years (45%), followed by 66 to 75 years (28%). They are 100% susceptible to amino glycosides (100%) and Piperacillin-Tazobactum (100%).The organisms showed very high susceptibility to 3rd generation Cephalosporins (100%), ciprofloxacin (100%), Amikacin (100%) and Azithromycin (100%).

Conclusion-The common organisms causing AECOPD in our study were gram negative organisms. Organisms isolated were Klebsiella followed by Pseudomonas aeruginosa. They were sensitive to aminoglycosides like gentamycin and Amikacin.

Keywords: Chronic obstructive pulmonary disease, acute exacerbations, antibiotic sensitivity

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the most predominant public health issue which is preventable and treatable and currently stands as the 4th leading cause of death in the world[1]. COPD is characterized by intermittent acute exacerbations associated with worsening symptoms and lung function[2]. It is the major cause of morbidity and mortality in the world and people die prematurely directly from it or complications arising out of COPD[3]. Chronic obstructive pulmonary disease is a group of progressive, debilitating respiratory conditions, including emphysema and chronic bronchitis, characterized by difficult breathing, lung airflow limitations, cough, and other symptoms[4]. The clinical course of COPD is punctuated by acute exacerbations that have been defined as ‘‘a sustained worsening of the patient’s condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient withunderlying COPD’’[5]. Exacerbations of COPD can be precipitated by several factors. The most common cause of exacerbations is respiratory tract infections either by virus or bacteria[3]and air pollution[6]. Exacerbations of

COPD are important events in the course of the disease because they negatively affect a patients quality of life[7], have effects on symptoms and lung function that can take several weeks to recover from[8], accelerate the rate of decline in lung function[9], are associated with significant mortality, particularly in those requiring hospitalization[3] and have high socioeconomic costs[10].

Finding bacterial pathogens causing AECOPD (Acute Exacerbation of Chronic Obstructive Pulmonary Disease) in the community is very important as specific antibiotic coverage can be used to prevent and also to treat the patients of AECOPD. A good knowledge about the common bacteria involved in acute exacerbations and their antibiotic sensitivity pattern would help in better management of such patients. So there is a need to find out the common bacterial pathogens causing Acute Exacerbations of COPD and their antibiotic sensitivity pattern in sputum culture in patients coming to tertiary care centre.

Aim

The aim of our study is to isolate bacterial pathogens in sputum culture of patients with acute exacerbation of COPD and sensitivity pattern of these pathogens.

Materials and methods-

A cross sectional observational studywas carried outbetween December, 2012 to June, 2014 at Konaseema Institute of Medical Sciences,Amalapuram. The sample includes a total of 60 AECOPD patients with positive sputum culture was taken in to the study after satisfying all the criteria. The following variables at admission were recorded: Age, Gender, Smoking status, Dyspnea, Cough with expectoration, Leucocytosis, fever and number of hospitalizations during the last 12 months. The study protocol was approved by the Institutional Ethical Committee (IEC). Informed consent was obtained from the patients.

Inclusion criteria:

All patients diagnosed to have AECOPD using Winnipeg criteria

- Increased sputum purulence
- Increased sputum volume
- Increased dyspnea

Exclusion criteria:

1) Individuals diagnosed with Bronchial Asthma, Pneumonia, Bronchiectasis.
2) All immune-compromised individuals
3) AECOPD patients with negative cultures
4) New and old TB cases
5) Patients who are already on antibiotics
6) Patients who are acutely ill.

Sample collection:

Two sputum samples were collected from each patient, one at the time of admission and the other early in the morning. The patients were nebulised with bronchodilator and after rinsing their mouth the sputum is collected. Some patients whose sputum was inadequate, a recollection of sputum was done after nebulisation with hypertonic saline. The patients were given a sterile wide mouthed disposable plastic bottle for the collection of the sputum. They were advised to collect deep coughed sputum after a deep inhalation. The sputum was sent to microbiology lab for culture and sensitivity. After culture report depending on the organism isolated, antibiotic sensitivity testing was done. Routine hematological investigations and chest x-ray were done on the day of presentation.The data was entered into Microsoft excel spreadsheet 2007 and analysed using IBM SPSS Version 16.0. Basic descriptive statistics were used to summarise the data.

Results

Out of 60 patients, 48(80%) were males and 12(20%) were females. The age group of the patients studied ranged from 45 to 82 years, the most common age group being 56 to 65 years (45%), followed by 66 to 75 years (28%).

Bacteriological profile

Out of 60 cultures from patients, 59 had single microbial infection and one patient had poly-microbial infection. On grams staining, 40 sputum samples were gram negative and 20 were gram positive. Graph 1

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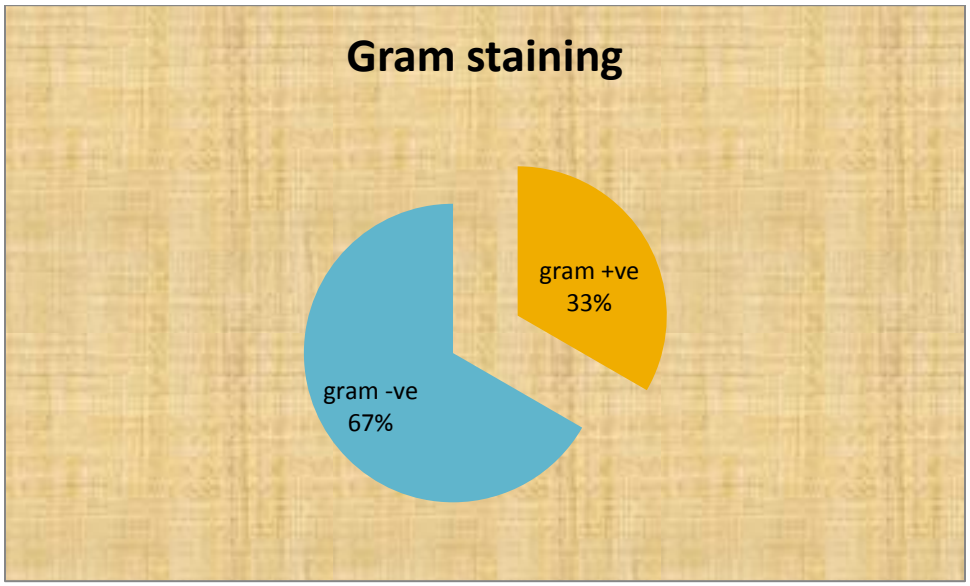
Graph.1- Pie chart showing percentage of gram positive (20) and gram negative (40) organisms



Organisms in gram positive cultures

The total number of gram positive organisms isolated is 20, the most common organism being Streptococcus pyogenes 7 (35%) and Staphylococcus aureus 7 (35%) and streptococcus pneumoniae was isolated in 6 patients(30%) .

Organisms in gram negative cultures

The total number of gram negative organisms is 40. The most common gram negative organism is Klebsiella pneumoniae 28 (71%) followed Pseudomonas aeruginosa 11(29%). One patient had poly microbial infection with these two gram negative organisms (Klebsiella pneumoniae & Pseudomonas aeruginosa).

Table.1 showing Antibiotic Sensitivity Pattern of Klebsiella

Antibiotic	Sensitive	Resistant	Total
Cefotaxime	6(35%)	11(65%)	17
Ceftrioxone	3(23%)	10(77%)	13
Cefixime	2(20%)	8(80%)	10
Cefoperazone	4(29%)	10(71%)	14
Ciprofloxacin	6(75%)	2(25%)	8
Norfloxacin	13(76%)	4(14%)	17
Lomefloxacin	14(67%)	7(23%)	21
Ofloxacin	17(65%)	9(35%)	26
Gentamycin	**12(80%)**	3(20%)	15
Tobramycin	**7(88%)**	1(12%)	8
Azithromycin	5(63%)	3(37%)	8
Clarithromycin	0	4(100%)	4
Clindamycin	0	3(100%)	3

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Amikacin	**19(86%)**	3(14%)	22
Amoxicillin-clav	2(15%)	11(85%)	13
Piperacillin-Tazobactum	17(77%)	5(23%)	22
Ampicillin-sulbactum	5(31%)	11(69%)	16
Tetracycline	**6(85%)**	1(15%)	7

Klebsiella was isolated in single culture in 28 patients. The sensitivity pattern showed that Klebsiella pneumoniae was most susceptible to Aminoglycosides(80-88%) followed by Tetracylcline (85%) and Piperacillin-Tazobactum(77%). Macrolides (0-63%) were least active followed by 3rd generation Cephalosporins (20-35%).

Table.2 showing Antibiotic Sensitivity Pattern of Pseudomonas

Antibiotic	**Sensitive**	**Resistant**	**Total**
Cefotaxime	5(63%)	3(37%)	8
Ceftrioxone	3(60%)	2(40%)	5
Cefixime	0	1(100%)	1
Cefoperazone	3(60%)	2(40%)	5
Ciprofloxacin	**7(88%)**	1(12%)	8
Norfloxacin	**2(100%)**	0	2
Lomefloxacin	0	2(100%)	2
Ofloxacin	1(20%)	4(80%)	5
Gentamycin	**8(100%)**	0	8
Tobramycin	**2(100%)**	0	2
Azithromycin	2(40%)	3(60%)	5
Clindamycin	0	2(100%)	2
Amikacin	**8(100%)**	0	8
Amoxicillin-clav	0	5(100%)	5
Piperacillin-Tazobactum	6(100%)	0	6
Ampicillin-sulbactum	1(25%)	3(75%)	4
Tetracycline	0	1(100%)	1

Pseudomonas sp cultures were isolated from 11 cultures. They are 100% susceptible to amino glycosides (100%) and Piperacillin-Tazobactum (100%). Flouroquinolones(20-100%) also show good amount of activity next to the above mentioned drugs. Cephalosporins (0-60%) show mixed activity. Table 2

Streptococcus pyogenes was isolated in 7 patients. These strains were found to be highly susceptible to Aminoglycosides (86-100%) and least susceptible to amoxicillin-clavulinic acid (20%) and Ampicillin-Sulbactum (50%). Piperacillin -Tazobactum (83%) also showed good activity again Streptococcus pyogenes. Cephalosporins (0-67%) showed mixed activity. Table 3

Table.3 showing Antibiotic Sensitivity Pattern of Streptococcus Pyogenes

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Antibiotic	Sensitive	Resistant	Total
Cefotaxime	4(57%)	3(43%)	7
Ceftrioxone	4(67%)	2(33%)	6
Cefixime	0	2(100%)	2
Ciprofloxacin	2(50%)	2(50%)	4
Ofloxacin	1(100%)	0	1
Gentamycin	**6(86%)**	1(14%)	7
Azithromycin	2(100%)	0	2
Clindamycin	0	4(100%)	4
Amikacin	**5(100%)**	0	5
Amoxicillin-clav	1(20%)	4(80%)	5
Piperacillin-Tazobactum	5(83%)	1(17%)	6
Ampicillin-sulbactum	1(50%)	1(50%)	2
Tetracycline	1(100%)	0	1

Streptococcus pneumonia was isolated in 6 patients. The organisms showed very high susceptibility to 3rd generation Cephalosporins (100%), ciprofloxacin (100%), Amikacin (100%) and Azithromycin (100%). But the organisms were 100% resistant to the Tobramycin and also to Ampicillin-sulbactum. Table 4

Table.4 showing Antibiotic Sensitivity Pattern of Streptococcus Pneumonia

Antibiotic	Sensitive	Resistant	Total
Cefotaxime	**6(100%)**	0	6
Ceftrioxone	**6(100%)**	0	6
Ciprofloxacin	3(100%)	0	3
Tobramycin	0	3(100%)	3
Azithromycin	**6(100%)**	0	6
Clindamycin	3(100%)	0	3
Amikacin	3(100%)	0	3
Amoxicillin-clav	3(100%)	0	3
Ampicillin-sulbactum	0	4(100%)	4

Table.5 showing Antibiotic Sensitivity Pattern of Staphylococcus Aureus

Antibiotic	Sensitive	Resistant	Total
Cefotaxime	**7(100%)**	0	7
Ceftrioxone	**5(100%)**	0	5
Cefoperazone	1(100%)	0	1

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Ciprofloxacin	2(40%)	3(60%)	5
Norfloxacin	1(100%)	0	1
Lomefloxacin	0	1(100%)	1
Ofloxacin	0	2(100%)	2
Gentamycin	**5(100%)**	0	5
Azithromycin	2(100%)	0	2
Amikacin	**6(100%)**	0	6
Amoxicillin-clav	5(83%)	1(17%)	6
Piperacillin-Tazobactum	2(100%)	0	2
Ampicillin-sulbactum	1(100%)	0	1

Staphylococcus aureus was isolated in 7 patients in total. The organisms were found to be highly susceptible to 3rd generation Cephalosporins (100%), Aminoglycosides (100%) and Piperacillin-Tazobactum (100%). The organisms showed high resistance to Ofloxacin and Lomefloxacin (100%). Table 5

Discussion

The main findings of the study were that the most common pathogens isolated in patients of AECOPD coming to tertiary care centre in amalapuram are Klebsiella pneumoniae, Pseudomonas, Streptoccoccus pneumoniae, Streptoccoccus pyogenes and Staphylococcus aureus. Gram negative organisms like klebsiella and pseudomonas were common organisms isolated. The gram positive organisms were Streptoccoccus pneumoniae, Streptoccoccus pyogenes and Staphylococcus aureus which were isolated in 6, 7, and 7 in numbers respectively. The number of Klebsiella pneumoniae isolated was 28 and Pseudomonas was 11. Most of the patients coming to the tertiary care centres use irregular antibiotics which are available over the counter during the study. Also these patients are pre-treated by Registered Medical Practitioners (RMP) who constitutes the main care givers in the rural areas in India. Another reason for non yielding of pathogens is AECOPD can be caused by viruses, atypical organisms, anaerobes and also environmental stresses. There are some disadvantages of culture from sputum as it can be contaminated with oropharyngeal secretions. Some studies used brochoscopic samples to culture the organisms, particularly for those requiring hospitalization or mechanical ventilation.[11,12,13] According to western literature the causative organisms for the AECOPD were H. influenza, streptococcus pneumonia, pseudomonas aeruginosa.

In a study done by Hallett Wibur[14] streptococcus pneumoniae and H.influenza were predominant.In a study by Eller Jorg, Anja Ede et al[15] showed that the predominant organisms causing AECOPD were streptococcus pneumoniae, non typeableH.influenza and to some extent Moraxella.In a study by De Abate Andrew C., et al[16] showed that the H.influenza, para influenza and Moraxella were predominant causative pathogens in AECOPD.

In a study conducted by Miravitlles Marc, Cristina Espinosa et al[13] shows H.influenza, pseudomonas and streptococcus pneumonia as the most common organisms causing AECOPD.

A study done by Hui DS, Ip M, et al[17] showed that gram-negative bacteria including Klebsiella pneumoniae,Pseudomonas aeruginosa and Acinetobacter baumannii. constitute a largeproportion of pathogens isolated in patients with AECB(Acute Exacerbation of Chronic Bronchitis) in some Asian countries. Surveillance on the local prevalence and antibiotic resistance of these organisms is important in guiding appropriate choice of antimicrobials in the management of AECB.

Our study is comparable to many Indian studies but different when compared to western studies. In contrast to western literature, Indian literature review

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shows no isolates of H. Influenza or Moraxella in AECOPD patients.

We used COPD-6 spirometer by Vitalograph to confirm the COPD status after improvement of the patient condition. Some patients showed FEV1/FVC values more than 0.70 as the patients are already on bronchodilators. It can be due to overlap syndromes. Patients with pseudomonas infection showed lower FEV1/FVC values compared to other infections. The COPD 6 spirometer is a hand held device which can be carried even to the bedside. It calculates the FEV1/FEV6 which corresponds to FEV1/FVC on normal spirometers.

A study of 100 cases by Pradhan K.C et al[18], shows Klebsiella pneumoniae to be the most predominant followed by staphylococcus aureus and pseudomonas.

In a study by Kamat SRet al[19] showed staphylococcus aureus, streptococcus pneumoniae, and klebsiella were most predominant organisms.

A study conducted by Arora Usha et al[20] shows the predominant organism isolated in AECOPD were staphylococcus aureus, Pseudomonas, Streptococcus pneumoniae and Klebsiella.

In our study of 60 patients the most predominant organisms causing AECOPD were gram negative Klebsiella, there were no isolates of H.influenza.

Klebsiella was isolated in 28(71%), Pseudomonas in 11(29%). This is in similarity with most of the studies that show a predominance of gram negative organisms. Antibiotics have to be started empirically to treat the presumed bacterial infection in AECOPD.

Aminopenicillins like ampicillin and amoxicillin were formerly the standard treatment in AECOPD. Due to emergence of resistance among respiratory pathogens their utility had been limited. Aminopenicillins with beta lactamase inhibitor is a better choice. Cephalosporins demonstrated clinical efficacy and tolerability that can surpass the standard aminopenicillins.

The quinolones like ciprofloxacin exhibit a broad spectrum of activity that includes both gram positive and gram negative organisms causing AECOPD. Ciprofloxacin was proven to be better than the newer quinolones in treating pseudomonas infection.

In our study we found that aminopenicillins were not effective against bothKlebsiella and Pseudomonas. Klebsiella was sensitive to Amikacin (86%) and Tobramycin(88%) Pseudomonas aeruginosa was sensitive to Amino glycosides (100%) and Piperacillin-Tazobactum (100%) and Ciprofloxacin (88%).

In a study done by Moellering, R. C[21] they found that Aminopencillins with beta-lactamase inhibitors were better than aminopencillins alone but were not effective in controlling severe infection in AECOPD due to beta lactamse producing strains.

A study done by Vogel.F[22] showsCephalosporins have demonstrated clinical efficacy and tolerability that compare well with or surpass those of the standard aminopenicillins with or without a beta-lactamase inhibitor.In a study done by Sethi.S[23] shows that the ciprofloxacin has excellent efficacy against the gram negative organisms.

Intravenous administration of third generation Cephalosporins and ciprofloxacin were the best antibiotics for treating less severe AECOPD patients empirically. Most of the organisms were susceptible to these antibiotics in our study also.

In severe infections as the organisms causing were likely to be gram negative organisms, a combination of Flouroquinolones and Aminoglycosides is the best antibiotic combination, alternatively a combination of intravenous third generation cephalosporin with Aminoglycosides can be used.But we have not correlated the severity with the organism isolated but it ispossible that majority of our patients had severe or very severe COPD as we hadincluded patients who needed hospital admission.Hence in future studies correlation with the severity of COPD, prior antibiotic use, comorbid illness needs to be correlated with the organism isolated.

The newer antibiotics like Pipericillin-Tazobactamwas very effective in treating very severe exacerbations of COPD. Routine use of this antibiotic has to be limited to prevent the emergence of resistance.

Conclusion

Exacerbations are episodes of acute worsening of clinical condition in patients with COPD. The common organisms causing AECOPD in our study

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were gram negative organisms. Organisms isolated were Klebsiella followed by Pseudomonas aeruginosa. They were sensitive to aminoglycosides like gentamycin and Amikacin. The gram negative organisms are resistant to first line antibiotics used in our institution. Hence all patients with AECOPD should be started on Piperacillin-Tazobactum or Aminoglycosides after renal function tests. These antibiotics are also highly active against streptococcus pyogenes which is one of the most common gram positive organisms in the study.

Limitations of the study

a) Testing of anaerobes was not done as they are difficult to grow and non availability of the media and take longer time than aerobes.
b) Contamination of sputum sample with oropharyngeal secretions lead to false results
c) Confirmation of COPD status with spirometry before treatment is difficult due to poor effort though it is confirmed after the treatment is done.

The study should be conducted on larger patient population to show significant findings of antibiotic activity.

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