A STUDY OF CORRELATION OF CLINICAL RESPONSE WITH MICROBIOLOGICAL SENSITIVITY IN COPD PATIENTS WITH ACUTE EXACERBATION

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ABSTRACT

BACKGROUND

The purpose of this study is to correlate the clinical outcome in patients of COPD with acute exacerbation with the bacteriology and culture sensitivity of the pathogens.

MATERIALS AND METHODS

This is a prospective study done in Government Fever Hospital/Guntur Medical College, Guntur from January 2014 to June 2015. The total number of patients included in the study was 100. Out of 100 patients, 94 (94%) were males and 6 (6%) were females. The mean age of the patients in this study was 56.8 years. The youngest patient was 39 years old and the oldest patient was 80 years old, giving an age range of 39 to 80 years. The study group consisted of patients already diagnosed as COPD who were admitted in Government Fever Hospital/Guntur Medical College, Guntur with features suggestive of acute exacerbation of COPD during the period from January 2014 to June 2015. The procedure workup consists of detailed clinical history along with chest x-ray PA view. If both of them satisfied the inclusion and exclusion criteria, then routine blood investigations including Hb%, RBC count, TLC and DLC are done and sputum is collected in a wide mouthed sterile sputum container.

RESULTS

The procedure workup consists of detailed clinical history along with chest x-ray PA view. If both of them satisfied the inclusion and exclusion criteria, then routine blood investigations including Hb%, RBC count, TLC and DLC are done and sputum is collected in a wide mouthed sterile sputum container.

CONCLUSION

Present study concludes that bacteria are major cause for AECOPD as bacteria were cultured in 92%. Sputum Gram stain examination gives immediate result, is a simple, reliable bed side tool in identifying the causative bacteria for AECOPD and also correlates with sputum cultures. Purulent sputum is an indication to initiate antibiotic therapy. The commonest bacteria isolated are *Streptococcus pneumoniae* (28%) followed by *Klebsiella pneumoniae* (20%). A control group of 20 patients with AECOPD have been selected and were initiated empirical antibiotic therapy without sputum examination for bacteriology. The result of clinical response have been studied. The present study also concludes that either oral or parenteral ampicillin will not benefit patients with bacterial cause of AECOPD. Quinolones and aminoglycosides are more effective in treating the bacterial exacerbation of the chronic obstructive pulmonary disease.

KEYWORDS

Acute Exacerbation of COPD (AECOPD), Culture Sensitivity, Gram Staining, Sputum Examination, Treatment Response in Patients with AECOPD.

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BACKGROUND

An exacerbation of the COPD is an acute event characterised by worsening of the patient's respiratory symptoms that is beyond normal day-to-day variation and lead to change in medication.⁽¹⁾ Exacerbation of COPD is important because it is associated with significant mortality, negatively affects the patient's quality of life and accelerates the decline in lung function. Exacerbations can be precipitated by the several risk factors. Clinical features of acute infection in

COPD include increased dyspnoea, productive cough. There may be fevers, chills, malaise, pleural chest pain and haemoptysis. The sputum's colour or thickness may change. It is difficult to diagnose 33 respiratory infections in a patient with AECOPD, because many of the symptoms and signs are present at baseline or can be seen in non-infectious exacerbations.

Chest x-ray should be taken to exclude alternative diagnosis. Spirometry should not be done to the patient with exacerbation, because the result is inconclusive and the patient has poor general condition. Haemogram, pulse oximetry, arterial blood gas analysis and electrocardiogram should be obtained to assess the severity of the exacerbation. Treatment of the exacerbation include increase in frequency and dose of inhaled or nebulised short-acting bronchodilators, either beta-2 agonists or anticholinergics. Intravenous methylxanthines may be used as second line agents. Corticosteroids improve lung function and shorten the recovery time.

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Antibiotics should be given to patients with all the cardinal signs of increase in dyspnoea, purulent sputum and copious amounts of expectoration. Selection of the antibiotic depends on local resistance pattern of the bacteria. Usual duration of the treatment is 5 - 10 days.⁽²⁾ Supplemental oxygen therapy, non-invasive or invasive ventilation should be considered in every patient with respiratory distress. Exacerbations can be prevented by protective measures against air pollution, cessation of smoking, pneumococcal and influenza vaccination in elderly and low mobility or poor reflexes like in Parkinson's disease or residual stroke. Use of phosphodiesterase-4 inhibitors like roflumilast has also been proposed. Knowledge about use of current medication and inhalation technique are vital in prevention of exacerbations.^(3,4) The risk of death from an exacerbation of COPD is closely related to the development of respiratory acidosis, the presence of serious co-morbidities and the need for ventilatory support. Patients without these features are not at high risk of death, but those with severe underlying COPD often require hospitalisation.⁽⁵⁾

Aims

1. To identify the specific pathogens causing an acute exacerbation in patients with previously diagnosed COPD patients in a cohort of 100 patients.
2. To correlate the clinical response in patients with AECOPD in study group with similar patients selected as control group.

Inclusion Criteria

Patient previously diagnosed as COPD having at least two of the following three symptoms were included in the study.

1. Increase in dyspnoea.
2. Increase in sputum production.
3. Increase in purulence of sputum.

Exclusion Criteria

1. Received antibiotics in the past four weeks.
2. Patients with infiltrates in chest x-ray.
3. Patients of cystic fibrosis, bronchiectasis, tuberculosis or other lung disease.
4. Sputum microscopy specimen with > 10% epithelial cells per low power field and < 25 polymorphs per low power field were not cultured.

MATERIALS AND METHODS

1. Disposable and sterilised wide mouthed sputum container.
2. Glass slides, 2 in number.
3. Nichrome loop wire and spirit lamp.
4. Sheep blood agar and McConkey plate.
5. Stains used in Gram's staining technique.
6. Antibiotic discs.

Methodology

Sputum Collection

The patient is advised to collect the sputum in wide mouthed sterile container provided at the time of admission. And this sputum container is transported to the Department of Microbiology, Guntur Medical College within half an hour.

Sputum Examination

In the Department, direct microscopy of the smear prepared from the sputum transported is examined under low power

field of the microscope. If the smear has < 10 epithelial cells and > 25 pus cells under low power field, then sputum inoculation is done.

Sputum Inoculation

One loop full of specimen is inoculated on to the surface of a well dried sheep blood agar plate and McConkey plate. The inoculum is distributed on the plates by a method called "surface plating" (technique streak culture). The streak culture technique consists of transferring the inoculum on to the surface of a well dried plate, on which it is spread over a small area at the 37 periphery. The inoculum is then distributed thinly over the plate by streaking it with the loop in series of parallel lines in different segments of the plate.

After inoculating the plates, Gram's staining is performed on the smear prepared from the sputum sample.

After incubating the plates at 37°C for 24 hrs., the colony characteristics on the inoculated plates were noted.

Colony Confirmation

The colonies obtained from the blood agar plate were confirmed by Gram staining.

The McConkey plate was also incubated overnight at 37°C and if there was any growth the colony characteristics were studied by Gram's Method and further confirmation was made by biochemical reactions (IMViC reactions and sugar fermentation).

Antibiotic Sensitivity Testing

By Modified Kirby-Bauer method, it was done by disc diffusion technique on Mueller Hinton agar.

Statistics

This is a prospective study done in Government Fever Hospital/Guntur Medical College, Guntur from January 2014 to June 2015. The total number of patients included in the study was 100.

Sex Distribution

Out of 100 patients 94 (94%) were males and 6 (6%) were females.

The mean age of the patients in this study was 56.8 years. The youngest patient was 39 years old and the oldest patient was 80 years old, giving an age range of 39 to 80 years. The following Table 7 and Figure 4 gives the age distribution of the patients in this study.

This is a prospective study done in Government Fever Hospital/Guntur Medical College, Guntur from January 2014 to June 2015. The total number of patients included in the study was 100.

Demographic Data

Sex Distribution

Out of 100 patients 94 (94%) were males and 6 (6%) were females.

RESULTS

An exacerbation of the COPD is an acute event characterised by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variation and lead to change in medication. Exacerbation of COPD is important because it is associated with significant mortality, negatively affects the patient's quality of life and accelerates the decline in the lung function. Exacerbations can be precipitated by several risk factors, mainly smoking and old age.

Antibiotics should be given to patients with all the cardinal signs of increase in dyspnoea, purulent sputum and copious amounts of expectoration. Selection of the antibiotic depends on local resistance pattern of the bacteria. Usual duration of the treatment is 5 - 10 days. Supplemental oxygen therapy, non-invasive ventilation should be considered in every patient with respiratory distress. Exacerbations can be prevented by protective measures against air pollution, cessation of smoking, pneumococcal and influenza vaccination in elderly and low mobility or poor reflexes like in Parkinson's disease or residual stroke. Aim of study is to identify the specific pathogens causing an acute exacerbation in patients with previously diagnosed COPD patients in a cohort of 100 patients. To correlate the clinical response in patients with AECOPD in study group with similar patients selected as control group.

The patient is advised to collect the sputum in wide mouthed sterile container provided at the time of admission. And this sputum container is transported to the Department of Microbiology, Guntur Medical College within half an hour. Meanwhile start antibiotics and wait for culture sensitivity, and we can change antibiotic accordingly to check clinical improvement.

Figure 1. Sex Distribution

Age Distribution

The mean age of the patients in this study was 56.8 years. The youngest patient was 39 years old and the oldest patient was 80 years old, giving an age range of 39 to 80 years. The following Table 1 gives the age distribution of the patients in this study.

Age	No. of Cases	Percentage of Total Cases (%)
31 - 40	4	4
41 - 50	28	28
51 - 60	36	36
61 - 70	20	20
71 - 80	12	12
Total	100	100

Table 1. Age Distribution

Risk Factor Evaluation

64 (64%) out of 100 patients of this study were current smokers, 28 (28%) patients were ex-smokers and 8 (8%) were non-smokers. All the females were non-smokers. Exposure to biomass fuel was present in all the female patients.

No. of Patients	Smoking Pattern		
	Smokers	Ex-Smokers	Non-Smokers
100	64 (64%)	28 (28%)	8 (8%)

Table 2. Smoking Pattern of Study Population

Symptoms

The most common symptom is cough with expectoration (100%).

Symptom	No. of Cases	Percentage (%)
Cough	100	100%
Expectoration	100	100%
Breathlessness	95	95%
Fever	52	52%
Chest pain	24	24%

Table 3

Sputum

The most common type of sputum obtained is mucopurulent in 80 (80%) patients followed by mucoid in 20 (20%) patients.

Type of Sputum	Cases	Total Cases	Percentage
Mucopurulent	80	100	80%
Mucoid	20	100	20%

Table 4. Sputum Microscopy

Type of Sputum	Cases	Isolation of Bacteria	Percentage Positivity (%)
Mucopurulent	80	80	100
Mucoid	20	12	60

Table 5. Bacterial Isolation from the Sputum Culture

Bacterial Growth	Cases	Total Cases	Percentage (%)
Positive	92	100	92
Negative	8	100	8

Table 6. Bacterial Growth in Sputum

Gram Staining Technique	Culture Positive in Correlation with Gram Stain	Percentage Positivity
Bacteria identified - 76	76	100%
No bacteria identified - 24	16	66.67%

Table 7. Comparison of Gram Stain and Culture

Bacteria identified	8	40%
No bacteria identified	12	60%

Table 8. Gram Stain Technique of Mucoid Sputum Gram Stain Technique of Mucoid Sputum (20)

Bacteria identified	68	85%
No bacteria identified	12	15%

Table 9. Gram Stain Technique of Mucopurulent Sputum Gram Stain Technique of Mucopurulent Sputum (80)

Total No.	Bacteria Identified by Gram Stain	Culture Positive	Type of Bacteria
20	8 (40%)	12 (60%)	Gram positive 8 (66.6%) Gram negative 4 (33.3%)

Table 10. Comparison of Gram Stain and Culture of Mucoid Sputum

Total No.	Bacteria Identified by Gram Stain	Culture Positive	Type of Bacteria
80	68 (85%)	80 (100%)	Gram positive 52 (65%) Gram negative 28 (33.3%)

Table 11. Comparison of Gram Stain and Culture of Mucopurulent Sputum

Bacteria	Number	Percentage (%)
Streptococcus pneumoniae	28	28
Klebsiella pneumoniae	20	20
β-Haemolytic Streptococci	20	20
Staphylococcus aureus	12	12
Pseudomonas aeruginosa	8	8
E. coli	4	4

Table 12. Bacteria Isolated in the Sputum Culture

Bacteria isolated in the sputum culture antibiogram (sensitivity pattern) of the bacteria isolated in the sputum culture is shown in the table.

Antimicrobial Agent	Drug Disc Concentration (mcg)	Number of Isolates %	
		Resistant	Susceptible
Streptococcus Pneumoniae (n=28)			
Ampicillin	10	20	8
Ceftriaxone	30	18	10
Tetracycline	30	12	16
Gentamycin	10	10	18
Amikacin	30	2	26
Levofloxacin	5	1	27
Klebsiella pneumonia (n = 20)			
Ampicillin	10	20	00
Ceftriaxone	30	08	12
Tetracycline	30	11	09
Gentamycin	10	06	14
Amikacin	30	1	19
Levofloxacin	5	1	19
β-Haemolytic Streptococci (n = 20)			
Ampicillin	10	16	04
Ceftriaxone	30	12	08
Tetracycline	30	15	05
Gentamycin	10	7	13
Amikacin	30	3	17
Levofloxacin	5	0	20
Staphylococcus aureus (n = 12)			
Ampicillin	10	12	00
Ceftriaxone	30	08	04
Tetracycline	30	07	05
Gentamycin	10	02	10
Amikacin	30	02	10
Levofloxacin	5	1	11
Pseudomonas Aeruginosa			

(n = 8)			
Ampicillin	10	08	00
Ceftriaxone	30	08	00
Tetracycline	30	02	06
Gentamycin	10	01	07
Amikacin	30	01	07
Levofloxacin	5	00	08
E. coli (n = 4)			
Ampicillin	10	04	00
Ceftriaxone	30	02	02
Tetracycline	30	03	01
Gentamycin	10	02	02
Amikacin	30	00	04
Levofloxacin	5	01	03

Table 13. Antibiogram of the Bacteria Isolated in Sputum Culture

Age (Years)	Clinical Outcome		
	Mean Duration of Stay (Days)	Deaths	Discharge with Home Oxygen Therapy
31 - 40	6	-	
41 - 50	7	-	
51 - 60	12	-	
61 - 70	10	-	3
71 - 80	15	-	3

Table 14. Clinical Outcome in Relation to Age

The average length of stay in the hospital was about 10 days. Length of stay increased with age. There is no mortality in our study. Only 6 (6%) patients were discharged with advice of home oxygen therapy.

We compared the clinical response of the study group with a control group of 20 patients who are also previously diagnosed with COPD now presented with clinical picture of acute exacerbation. The control group patients have been subjected to laboratory tests and were given empirical treatment without any sputum examination. The response is tabulated as under.

Group	Fever	Sputum Production	Breathlessness
Study Group (100)	5 - 7 days	7 - 10 days	4 - 5 days
Control Group (20)	10 - 12 days	14 - 18 days	7 - 10 days

Table 15. Symptomatology Distribution

Comparison with other Studies

Study	Year	Mean Age (Years)
R.I.M. El Korashy et al	2012	62.6
Saikat Basu et al ⁽⁶⁾	2012	54.88 ± 8.82
White et al ⁽⁷⁾	2003	52 years
Shahnawaz A et al ⁽⁸⁾	2003	59.42 ± 10.59
Present Study	2014 - 2015	56.8

Table 16. Comparison of Mean Age

Study	Year	Male-to-Female Ratio
Saikat Basu et al ⁽⁶⁾	2012	3.2:1
Fanny WS et al	2005	3.7:1
Xiuqing Ma et al	2013 - 2014	1.83:1
Xue-Jun Li et al	2007 - 2008	2.48:1
Khaled Eid Sobhy et al	2010 - 2013	10:1
R.I.M. El Korashy et al	2013	12.5:1
Levent Erkan et al	1999 - 2002	17.75:1
Present Study	2014 - 2015	15.66:1

Table 17. Comparison of Male-to-Female Ratio

Author	Year	No. of Patients	Percentage of Patients with Positive Results
Vesna Cukic	2012	75	31%
Anand K Patel et al	2011-2012	50	82%
Mandira Varma Basil et al	2004-2006	100	16%
Fanny WS	2005	329	37.8%
Luigi et al	2004	581	90.7%
Roche et al	2003	118	59%
Monso et al	2003	90	43.3%
White et al ⁽⁷⁾	2003	54	88.88%
Pela et al	1998	40	84%
Present Study	2014-2015	100	92%

Table 18. Comparison of Percentage of Patients with Positive Sputum Culture

Study	Year	Most Common Bacteria Isolated
Vesna Cukic	2012	Streptococcus pneumoniae
Anand K Patel et al	2011-12	Streptococcus pneumoniae
Saikat Basu et al	2012	Klebsiella pneumoniae
Shahnawaz A et al	2003	Pseudomonas aeruginosa
White et al ⁽⁷⁾	2003	Haemophilus influenzae
Fanny WS et al	2005	Haemophilus influenzae
Xiuqing Ma et al	2013 - 14	Klebsiella pneumoniae
Xue-Jun Li et al	2007 - 08	Pseudomonas aeruginosa
Khaled Eid Sobhy et al	2010 - 13	Klebsiella pneumoniae
R.I.M. El Korashy et al	2012 - 13	Pseudomonas aeruginosa
Levent Erkan et al	1999 - 2002	Haemophilus influenzae
Mandira Varma Basil et al ⁽⁹⁾	2004-06	Streptococcus pneumoniae
Luigi et al	2004	Streptococcus pneumoniae
N Arora et al ⁽¹⁰⁾	2001	Streptococcus pneumoniae
Saira Furqan et al	2009-10	Streptococcus pneumoniae
Gerard Rakesh et al ⁽¹¹⁾	2013	Streptococcus pneumoniae
Pela et al	1998	Streptococcus pneumoniae
Present study	2014-15	Streptococcus pneumoniae

Table 19. Comparison of Most Common Bacteria Isolated in Sputum Culture

Study	Year	Most Effective Antibiotic
Xiuqing Ma et al	2013 - 14	Tigecycline
Gerard Rakesh et al ⁽¹¹⁾	2013	Amikacin
R.I.M. El Korashy et al	2012 - 13	Imipenem
Saikat Basu et al ⁽⁶⁾	2012	Amikacin
Khaled Eid Sobhy et al	2010 - 13	Imipenem
Madhavi S et al	2011-2012	Amikacin
Saira Furqan et al	2009-10	Levofloxacin
Xue-Jun Li et al	2007-08	Levofloxacin
Shahnawaz A et al ⁽⁸⁾	2003	Levofloxacin, Amikacin
L. Davis et al ⁽¹²⁾	2001	Co-Amoxiclav
Levent Erkan et al	1999-2002	Ciprofloxacin
Present Study	2014 - 15	Levofloxacin, Amikacin

Table 20. Comparison of Most Effective Antibiotic

Summary

- Majority of patients are in the age group of 39 - 80 years.
- Out of 100 people, 94% are males and 6% are females.
- Most common presenting symptoms are cough (100%) and expectoration (100%) followed by breathlessness (95%).
- Out of 100 people, 64 (64%) patients are current smokers, 28 (28%) are ex-smokers and 8 were non-smokers.
- The most common type of sputum obtained is mucopurulent in 80 (80%) patients followed by mucoid in 20 (20%).
- Mucopurulent sputum has been seen in 80 (80%) cases, in which Gram's stain identified bacteria in 68 (85%) cases and culture isolated bacteria in all 80 (100%) cases.
- Mucoid sputum has been seen in 20 cases, Gram's stain identified bacteria in 8 (20%) cases and culture is positive in 12 (60%) cases.
- The commonest bacteria isolated in sputum culture is Streptococcus pneumoniae (28%) followed by Klebsiella pneumoniae (20%).
- Bacterial pathogens isolated in our study are more sensitive to levofloxacin (95%) followed by amikacin (91%).
- The clinical response in the case study group is early, predictive and early as compared to the control group.

DISCUSSION

In our study, the study group consists of 100 patients. The mean age of patients in our study is 56.8 years. This is comparable to studies undertaken by L. Davis et al⁽¹²⁾ (50 years), White et al⁽⁷⁾ (52 years), Fanny et al⁽¹⁰⁾ (74.4 + 8.3 years), N Arora et al⁽¹⁰⁾ (47.36 + 11.25 years), Shahnawaz A et al⁽⁸⁾. Most of the subjects (36%) in our study falls in the age group of 51 - 60 years, which is comparable to studies undertaken by N Arora et al⁽¹⁰⁾ in which 67% of people are in the age group of 50 - 60 years, Saikat Basu et al⁽⁶⁾ in which 38% of people falls in the age group of 55 - 65 years and Gerard Rakesh et al (54), in which 43% of the subjects falls in the age group was 50 - 55 years.

Marc Miravittles

1999 from Spain culture sputum samples from 91 patients and isolated Haemophilus influenzae 20 cases, Pseudomonas aeruginosa 14 cases and Streptococcus pneumoniae 9 cases, Moraxella catarrhalis 8 cases. The other being gram negative

bacteria 7 cases.⁽¹³⁾

Breathlessness on exertion, sometimes accompanied by wheeze and cough, which is often but not invariably productive are the characteristic symptoms of COPD. Reversibility tests are important in COPD to distinguish those patients with marked reversibility who have underlying asthma, because of FEV1 after bronchodilator is the best predictor of survival.⁽¹⁴⁾ Questioning usually reveals the presence of a 'smoker's cough' with the production of small amounts (usually < 60 mL) of mucoid sputum, often occurring predominantly in the morning for many years.

The major presenting symptoms in our study are worsening of cough and expectoration in 100% of the patients, 95% of the patients are presented with worsening of breathlessness, 52% of people have fever and 24% of patients have chest pain on the day of admission. This was comparable to the study undertaken by Mandira Varma Basil et al,⁽⁹⁾ in which 90% of people presented with worsening of breathlessness.

Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of death in the world and expected to be the third leading cause of death by year 2030, represents an important public health challenge that is both preventable and treatable.⁽¹⁵⁾ Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.⁽¹⁶⁾

CONCLUSIONS AND PROPOSALS

1. Our study concludes that the AECOPD patients suffer from deterioration of general condition and respiratory function, which leads to increased morbidity. Many working days are lost and there is a definite deterioration of quality of life index. Moreover, as the patient is elderly the attendants also must lose their active working days to take care of the sick.
2. The clinical response must be early and effective. This must be re-evaluated in a demographic area periodically by the health care personnel.
3. The microbiological study with culture specific antibiotic is the best, though it takes a prolonged time of one week. The bedside Gram staining examination of sputum may be offered as an equally specific test.
4. There may be some alterations in the type of bacteria that cause AECOPD and their pharmacological response at the community level.
5. Our study offers a reference for the spectrum of antibiotics that are most effective, hence will be of high value both at the teaching hospital and rural healthcare facilities.
6. We propose such studies in the referral teaching hospital as multidisciplinary care is available to be done periodically to provide vital information regarding the pattern of respiratory diseases.

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