EVALUATION OF CLINICAL, DIAGNOSTIC AND TREATMENT OUTCOME IN ACUTE EXACERBATION OF BRONCHIECTASIS IN ADULTS

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ABSTRACT

BACKGROUND

Bronchiectasis is defined as "abnormal and permanent dilatation of one or more bronchi due to weakening or destruction of the muscular and elastic components of the bronchial walls." HRCT has become the gold standard to diagnose bronchiectasis. Antibiotics and chest physiotherapy are main forms of management.

The aim of the study is to study the outcome of treatment in acute exacerbation of bronchiectasis in adults.

MATERIALS AND METHODS

This study was done prospectively in the Department of Respiratory Medicine in Rajarajeswari Medical College and Hospital from November 1, 2015, to April 30, 2017. Out of 55 cases admitted during the study period, 44 cases (10 females) were eligible for participation in the study. 2 cases of Kartagener's syndrome under follow up in our department for past 3 years were included. Flexible bronchoscopy was done in 31 patients.

RESULTS

Cough with sputum was the commonest symptom. Breathlessness was documented in 32 patients. Arterial blood gas analysis was abnormal in 29 patients. Haemoptysis in 13 cases. History of antituberculous therapy was present in 34 patients. Digital clubbing was present in 30 patients. Pedal oedema was documented in 14 cases. Associated cultures were positive in 28 cases.

CONCLUSION

The most frequent form of bronchiectasis is post-tuberculous. Pseudomonas aeruginosa is the most frequently isolated bacteria. The most frequent concomitant disease in bronchiectasis is COPD. Piperacillin/tazobactum is the most effective antibiotic for initial empirical treatment of acute exacerbations of bronchiectasis.

KEYWORDS

Bronchiectasis, Bronchial Walls, Chest Physiotherapy.

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BACKGROUND

Bronchiectasis is a relatively common disease in a developing country like India and in western countries. It is limited to homeless and poor people (orphan's disease).[1] First known description of bronchiectasis given by Laennec in 1819[2] and pathological classification of bronchiectasis was done by Reid.[3]

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Bronchiectasis once established is permanent and is defined as "abnormal and permanent dilatation of one or more bronchi due to weakening or destruction of the muscular and elastic components of the bronchial walls."[4] Bronchiectasis maybe congenital or acquired. Bilateral bronchiectasis occurs more often as a result of congenital abnormality or in association with a systemic disease.[4]

Bronchiectasis may occur due to inadequately treated infections or due to virulence of the organisms. A wide variety of conditions predispose to development of bronchiectasis (Table 1). Various causative organisms are involved (Table 3). Infection with pseudomonas aeruginosa may be problematic as they produce biofilms, which increases their virulence by preventing phagocytosis and promotes disease progression leading to higher morbidity and mortality.[5] Patients with history of gastroesophageal reflux have increased risk of aspiration and that the

organism Helicobacter pylori may have a role in the development of bronchiectasis.[6,7,8] Inhalation of noxious fumes and particulate matter is also associated with bronchiectasis.[9] Cystic fibrosis is the most common cause of bronchiectasis in the United States and other developed countries.[10] Primary ciliary dyskinesia is a group of inherited disorders that may affect 1 in 15,000-30,000 persons. It is manifested by immotile cilia of the respiratory tract and/or sperm.[11,12] A variant of this condition initially described by Kartagener consists of the clinical triad of situs inversus, nasal polyps or sinusitis and bronchiectasis in the setting of immotile cilia of the respiratory tract.[13] The resulting bronchiectasis in ABPA is thin-walled and affects the central and medium-sized airways.[14] Immune deficiencies causing bronchiectasis include hypogammaglobulinaemia, immunoglobulin G (IgG) subclass deficiency; selective immunoglobulin A (IgA), immunoglobulin M (IgM) or IgE deficiency. Bronchopulmonary sequestration is a congenital abnormality classified as either intralobar or extra lobar and results in chronic lower respiratory tract infections that lead to bronchiectasis.[15,16,17] Williams-Campbell syndrome or bronchomalacia is the absence of cartilage from lobar to first- to second-generation segmental airways that results in extensive peripheral bronchiectasis.[18] Mounier-Kuhn syndrome or tracheobronchomegaly is a rare disorder caused by atrophy or complete absence of elastic fibres and thinning of muscular components of the airway.[19] Marfan syndrome is a connective-tissue disorder in which the weakness of the connective tissue of the bronchial wall predisposes to bronchiectasis.[20] Yellow nail syndrome is a triad of yellow atrophic nails, lymphedema and chronic pulmonary disease.[21]

Rheumatoid arthritis is associated with bronchiectasis is reported in 3.2-35% of patients and associated with poor prognosis.[22,23] Sjogren's syndrome maybe secondary to increased viscosity of mucus and impaired airway clearance.[24] SLE may present with a variety of pulmonary manifestations including bronchiectasis.[25] Bronchiectasis has been reported in both ulcerative colitis and Crohn's disease.[26]

Clinically, most cases of bronchiectasis present with chronic persistent or intermittent cough with sputum production. The sputum maybe mucoid, mucopurulent or purulent.[27] Haemoptysis[28,29] occurs in some patients and maybe minimal-to-severe in some cases. Breathlessness[28] occurs in a vast majority of patients. Systemic symptoms include fever, chest pain, loss of appetite, patients with mild bronchiectasis may not have any physical signs between exacerbations, whereas patients with moderate-to-severe bronchiectasis have physical signs on examination such as digital clubbing, coarse crackles on auscultation and occasionally evidence of respiratory failure and cor pulmonale.[28]

Acute exacerbations are characterised by deterioration of respiratory symptoms, which includes increased volume and purulence of sputum and increased breathlessness with or without fever. The sputum may have offensive odour if anaerobic infections are associated. In a study by O'Donnell et al,[25]an acute exacerbation of bronchiectasis was defined when four or more of the following symptoms were present. The symptoms are change in sputum production, increased dyspnoea, increased cough, fever, increased wheezing, constitutional symptoms such as malaise, fatigue, lethargy, reduced pulmonary function, radiographic changes consistent with a new pulmonary process and change in chest sounds. Bronchiectasis can be divided into four types[3] - cylindrical bronchiectasis, which is characterised by uniform dilatation of bronchi without any tapering. Varicose bronchiectasis characterised by beaded appearance due to alternating dilatation and constriction of bronchi. Cystic or saccular bronchiectasis is the most severe form characterised by peripheral bronchial dilatation to form large cysts with air fluid levels. Follicular bronchiectasis is characterised by extensive lymphoid follicles within the bronchial walls and this type usually occurs following childhood infections. HRCT has become the gold standard to diagnose bronchiectasis.[30]

Aim- To study the outcome of treatment in acute exacerbation of bronchiectasis in adults.

MATERIALS AND METHODS

This study was done prospectively in the Department of Respiratory Medicine in Rajarajeswari Medical College and Hospital from November 1, 2015, to April 30, 2017. The study protocol was approved by institutional ethics committee. Before enrolling into the study, written informed consent was obtained from all the patients. Consecutive cases of bronchiectasis of 18 years and above of either sex admitted with acute exacerbations have been studied. Two cases of Kartagener's syndrome under follow up in our department for past 3 years were also included. The acute exacerbation of bronchiectasis was made through pre-existing criteria.[31] Patients were considered to have mild sputum if they produced less than 10 mL in 24 hours, moderate sputum if they produce 10 to 150 mL and copious sputum if they produce more than 150 mL in 24 hours. Out of 55 cases admitted during the study period, 44 cases (10 females) were eligible for participation in the study. The age of patients ranged from 18 to 72 years (average age 48.36). All cases were subjected to clinical examination, arterial blood gas analysis, urine and blood examination, blood chemistry, blood cultures, alpha-1 antitrypsin levels, sputum examination (smears and cultures for bacteria and mycobacteria). Flexible bronchoscopy was done in 31 patients and bronchoscopic specimens like bronchial washings were examined by smear and culture for bacteria and mycobacteria. In addition, spirometry (n-20) and transthoracic 2D echocardiogram (n-31) were done in selected patients. Immunoglobulin profile done included IgE measurement in patients (n-8) with history of asthma. Measurement of other immunoglobulins like IgM and IgG was not possible. Sperm count was done for three cases including Kartagener's syndrome. Since electron microscopy facility is

not available in our hospital, we used saccharin test to know the abnormalities of airway cilia in all nontuberculous bronchiectasis cases.

The treatment included oxygen therapy, broad range antibiotics, systemic steroids, nebulised bronchodilators (levosalbutamol) along with other supportive treatment. The details of broad range antibiotics used are shown in table No. 7 and 8. Chest physiotherapy was started as soon as possible in most cases. Patient was declared as not improved, if they had persistent symptoms even after 3 weeks of treatment.

RESULTS

The demographic details of the patients studied is shown in table 2. 31 cases (70.45%) had bronchiectasis of more than 5 years duration and 13 cases (29.54%) had the disease of less than 5 years. Acute exacerbations was more frequent in longstanding cases of bronchiectasis. Cough with sputum was the commonest symptom and was present in all cases. Sputum volume was moderate in 25 cases (56.81%) and copious in 19 cases (43.18%). Shortness of breath was documented in 32 patients (72.72%) and arterial blood gas analysis was abnormal in 29 patients (65.90%). Increased wheezing was documented in 21 patients (47.72%). Haemoptysis was documented in 13 cases (29.54%) and none of them had massive haemoptysis. Elevated body temperature of more than 39°C was noted in 28 patients (63.63%). History of antituberculous therapy was present in 34 patients (77.27%) suggesting post-tuberculous bronchiectasis. History of tobacco smoking was present in 23 patients (52.27%) including all cases of COPD.

56% of the patients had Body Mass Index (BMI) between 17-19 kg/m^2 and none had BMI of above 25 kg/m^2. Digital clubbing was documented in 30 patients (68.18%) and cyanosis was documented in 3 cases (6.81%). Pedal oedema was documented in 14 cases (31.81%). The physical finding showed presence of persistent coarse crackles in 40 cases (90.9%). Associated rhonchi was documented in 28 cases (63.63%). High-pitched bronchial breath sounds was documented in 7 cases (15.90%). Blood examination documented leucocytosis in 29 patients (65.90%) and hypoproteinaemia (less than 3 g/dL) in 20 cases (45.45%). Details of sputum smears are shown in Table 3. Bacterial cultures were read at the end of 72 hours. Cultures (sputum and bronchial washings) were positive in 28 cases (63.63%). The most common organism isolated was pseudomonas aeruginosa. Those who underwent flexible bronchoscopy, bronchial aspirates had growth of bacteriae on culture in 6 including 4 whose sputum cultures were sterile. Two patients admitted in intensive care unit underwent flexible bronchoscopy only for bacterial culture. Pseudomonas aeruginosa was present in four patients and Acinetobacter in one and streptococcus pneumonia along with pseudomonas in one patient. Pseudomonas was also the most common organism to be isolated in bronchial washings. Details of bacterial cultures is shown in Table 4. Sperm count was normal in all cases (n-3). Saccharin test was normal in all nontuberculous bilateral bronchiectasis except in both cases of Kartagener's syndrome. X-ray of paranasal sinuses was done and normal in all cases of post-tuberculous bronchiectasis (n-34) and abnormal in four cases of bilateral bronchiectasis including two cases of Kartagener's syndrome. The abnormalities in sinus x-ray included maxillary sinusitis in one case and pansinusitis in other three cases. Abnormal chest x-ray features were seen in 37 patients and details are shown in Table No. 5a and 5b. Echocardiogram showed features of cor pulmonale in 9.09% cases including both patients directly admitted into ICU. HRCT thorax was done in all cases and the details are shown in Table 6. The most frequent finding through HRCT thorax was bilateral bronchiectasis and was seen in 54.54%.

Antibiotic therapy involved use of 2 or more broad range drugs in all cases. Details of antibiotics used are shown in Table 7 and 8. 41 patients improved symptomatically and could be discharged within 3 wks. 2 patients (4.54%) died within 1 week while on treatment in intensive care unit. One patient (2.27%) did not improve even after three weeks and discharged himself against medical advice. Adverse effects of antibiotics were reported in 8 patients (18.18%) of which 2 patients had headache and 6 patients had mild nausea and epigastric pain. There were no serious side effects. Complications were seen in 3 patients (6.81%) and included ARDS in one patient who was directly admitted into intensive care unit, sepsis in 2 patients, of which one patient was directly admitted into intensive care unit while the other patient recovered.

Focal Distribution	
Bronchial obstruction	Foreign body Tumour Broncholithiasis Compression by peribronchial lymph nodes
Previous pneumonia	
Diffuse distribution	
Primary infective insult	
Impairment of mucus clearance	Cystic fibrosis Primary ciliary dyskinesia
Reduced host immunity	Congenital and acquired hypogammaglobulinaemia HIV infection
Hyperimmune response	ABPA
Autoimmune diseases	Inflammatory bowel disease SLE Rheumatoid arthritis Coeliac disease Cryptogenic fibrosing alveolitis
Inhalational/aspiration injury	Toxic fumes Gastric contents
Developmental defects	Pulmonary agenesis Sequestrated segment Tracheobronchomegaly Bronchomalacia Alpha-1 antitrypsin deficiency

Table 1. Factors Predisposing to Bronchiectatis[37]

Age Group	No. of Patients	Males	Females
18-30	10	7	3
31-50	8	5	3
51-64	18	14	4
65 and above	8	8	-

Table 2. Demographic Data

Sl. No.	Organism	No. of Patients
1.	Mixed	25
2.	Gram positive	1
3.	Gram negative	10
4.	Pus cells	8

Table 3. Sputum Smear Examination (Gram Stain Technique)

Single Organism - 17		Multiple Organisms - 11	
Pseudomonas aeruginosa	10	Streptococcus pneumoniae Pseudomonas aeruginosa	4
Klebsiella pneumoniae	3	Streptococcus pneumoniae Klebsiella pneumoniae	2
Acinetobacter	2	Streptococcus pneumoniae Acinetobacter	2
Moraxella catarrhalis	1	Moraxella catarrhalis Pseudomonas aeruginosa	2
Staphylococcus aureus	1	Klebsiella pneumoniae Pseudomonas aeruginosa	1

Table 4. Culture Reports of Sputum and Bronchial Washings

Sl. No.	Findings	No. of Patients
1.	Bilateral	24 (64.86%)
2.	Unilateral	13 (35.13%)
	Right side	6
	Left side	7

Table 5a. Chest X-Ray Abnormalities

Sl. No.	Findings	No. of Patients
1	Normal	7
2	Fibrotic lesions with volume loss	6
3	Fibrotic lesions with calcified foci and volume loss	9
4	Cystic lucencies	3
5	Hyperinflated lung fields with bronchiectatic changes	11
6	Hyperinflated lung fields with interstitial opacity	1
7	Hyperinflated lung fields with consolidation	1
8	Consolidation	2
9	Bronchiectatic changes	4

Table 5b

Sl. No.	Findings	No. of Patients
1.	Bilateral disease	24 (54.54%)
2.	Unilateral disease	20 (45.45%)
	Right side	13 (65%)
	Left side	7 (35%)
3.	Only upper lobes	24 (54.54%)
	B/L upper lobes	16
	Right upper lobe	5
	Left upper lobe	3
4.	Only lower lobes	10 (22.72%)
	B/L lower lobe	6
	Left lower lobe	3
	Right lower lobe	1
5.	Right upper lobe with middle lobe	3
6.	Left upper lobe with lingula	2
7.	Involvement of more than two lobes	2
8.	Associated with emphysema	14 (31.81%)

Table 6. Distribution of Bronchiectasis in HRCT Thorax

Beta-Lactam Antibiotics		No. of Patients
1.	Piperacillin/tazobactum	19
2.	Amoxicillin/clavulanic acid	7
3.	Meropenem	2
Aminoglycosides		
1.	Amikacin	11
2.	Gentamycin	7
Fluoroquinolones		
1.	Ciprofloxacin	3
2.	Levofloxacin	10
Cephalosporins		
1.	Ceftriaxone	5
2.	Cefepime	7
3.	Cefoperazone-sulbactam	8
Macrolides		
1.	Azithromycin	8
2.	Clarithromycin	5
Oxazolidinone		
1.	Linezolid	1
Lincosamide		
1.	Clindamycin	3

Table 7. Antibiotics Used

1.	Piperacillin/tazobactum + levofloxacin	2
2.	Piperacillin/tazobactum + amikacin	4
3.	Piperacillin/tazobactum + clarithromycin	3
4.	Piperacillin/tazobactum + gentamycin	1
5.	Piperacillin/tazobactum + azithromycin	3
6.	Piperacillin/tazobactum + ciprofloxacin	1
7.	Amoxicillin/clavulanic acid + levofloxacin	4
8.	Amoxicillin/clavulanic acid + gentamycin	2
9.	Amoxicillin/clavulanic acid + linezolid	1
10.	Cefoperazone/sulbactam + amikacin	1

11.	Cefoperazone/sulbactam + levofloxacin	2
12.	Cefoperazone/sulbactam + ciprofloxacin	1
13.	Cefoperazone/sulbactam + gentamycin	1
14.	Cefoperazone/sulbactam + clarithromycin	2
15.	Cefoperazone/sulbactam + azithromycin	3
16.	Ceftriaxone + levofloxacin	1
17.	Ceftriaxone + azithromycin	1
18.	Ceftriaxone + amikacin	2
19.	Ceftriaxone + gentamycin	1
20.	Cefepime + amikacin	1
21.	Cefepime + azithromycin + amikacin	1
22.	Piperacillin/tazobactum + amikacin + clindamycin	1
23.	Piperacillin/tazobactum + ciprofloxacin + gentamycin	1
24.	Piperacillin-tazobactum + clindamycin + gentamycin	1
25.	Meropenem + clindamycin + amikacin	2

Table 8. Combinations of Antibiotics Used

DISCUSSION

In a developing country like India, still cases of bronchiectasis continue to get admitted frequently with acute exacerbations.[33] In our study, copious purulent sputum was observed in 43.18% cases only. Sputum was foul smelling in 36.36% of cases. In our study, haemoptysis[28] occurred in 29.54% of cases and none had massive haemoptysis. In bronchiectasis, 50% of cases may have concomitant COPD.[33] In the present study, arterial blood gases were abnormal in 65.90% cases and in all cases of bronchiectasis with COPD. In our study, HRCT of chest showed features of emphysema along with bronchiectatic lesions in 31.81% of cases. Spirometry was done in 12 out of 14 cases of concurrent COPD and all revealed obstructive defect with poor reversibility. Various studies[34,35] showed post-tuberculous bronchiectasis to be the commonest cause of bronchiectasis. In our study also post-tuberculous bronchiectasis was the most frequent form of bronchiectasis. In developed countries where tuberculosis is less prevalent, idiopathic bronchiectasis continues to be the most common form.[29] In our study, 95% cases of bronchiectasis were acquired. With regard to detection of ciliary abnormalities, electron microscopy is not available in our institute and we relied on saccharin test in cases of non-tuberculous bronchiectasis (n-10). The diagnosis of Kartagener's syndrome (n-2) was made earlier. HRCT of chest is currently the gold standard for diagnosis of bronchiectasis.[30] In our case, bronchiectasis was diagnosed in all cases through HRCT of thorax. Initial chest x-ray was normal in 7 (15.90%) cases and as per literature chest x-ray can be normal in 10% of cases of bronchiectasis.[29] Regarding microbiological studies in bronchiectasis, haemophilus influenza was the most frequent organism isolated in previous studies.[36,37,32] In our study, pseudomonas aeruginosa was the most frequent single organism isolated. The bacterial culture was sterile in 16 cases (36.36%). The other reason could be viral exacerbations, which could not be detected. In patients with minimal sputum and localised bronchiectasis, non-pseudomonal antibiotic such as third generation intravenous cephalosporins and beta-lactam with a beta-lactamase inhibitor or macrolides are considered enough and in case of patients having moderate-to-copious sputum production and poor lung function, empiric anti-pseudomonal antibiotics such as intravenous ceftazidime or aminoglycosides and quinolones such as ciprofloxacin are advised. Underlying disease is the most common cause of death in acute exacerbations of bronchiectasis and was reported in 28% of cases.[38] In our study, only 2 patients died (4.54%). This low mortality rate maybe the result of early effective antibiotic therapy.

CONCLUSION

The most frequent form of bronchiectasis is post-tuberculous. Acute exacerbation of bronchiectasis manifests with copious sputum in 43.18% of cases; foul-smelling sputum in 36.36%. Pseudomonas aeruginosa is the most frequently isolated bacteria in bronchiectasis. Therefore, in acute exacerbation of bronchiectasis with copious sputum production, antipseudomonal antibiotics can be started prior to culture reports. The most frequent concomitant disease in bronchiectasis is COPD. HRCT of chest showed features of emphysema along with bronchiectatic lesions in 31.81% of cases. Piperacillin and tazobactum is the most effective antibiotic used in combinational therapy for initial empirical treatment of acute exacerbations of bronchiectasis with copious sputum production. Complication rate in acute exacerbation of bronchiectasis is 6.81% with 4.54% mortality.

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