

Acute exacerbation of chronic obstructive pulmonary disease in older people

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Abstract

The Chronic Obstructive Pulmonary Disease (COPD) is common in older people residing in rural India both in Men and Women. The Environmental and Domestic pollution apart from smoking tobacco has led to increased incidence of COPD. The World Health Organisation reports that the COPD is fourth leading cause of death worldwide. The misuse of steroids is very common in older people with COPD which leads to osteoporosis and bone fractures. Each exacerbation proves to be a costly affair for the family and it leads to decreased quality of life among the older people. The non-pharmacological measures like pulmonary rehabilitation, palliative care and end of life care are of paramount importance in older people and should be initiated in initial stages itself. Immunization against influenza and pneumococci prevents exacerbations and need to be practiced by all clinicians.

Keywords: Acute exacerbation, COPD, Older people.

Introduction

Chronic obstructive pulmonary disease (COPD) is characterised by the slowly progressive impairment of airflow in lung function and worsening of breathlessness, exercise capacity and impairment of quality of life with time.^{1,2} Exacerbations are acute worsening of clinical condition in COPD patients.

Prevalence

The high prevalence of COPD has made the disease a leading cause of morbidity and mortality worldwide which induces an economic and social burden³ AECOPDs account for the largest proportion of the COPD burden on the healthcare system. The National Commission on Macroeconomics and Health (NCMH) estimates of prevalence of COPD showed that burden of COPD were found to be more in rural India and would be increasing all the time.⁴

AECOPDs account for the largest proportion of the COPD burden on the healthcare system. Murthy KJR et al estimated that COPD could cause an economic burden of up-to Rs 56 billion in 2016 based on the estimates made during 2001-2005 assuming that the practice of treating COPD would remain same⁽⁴⁾.

Issues Specific for Older People

Treating AECOPD and associated co morbidities require institutional resources and regular hospitalizations which can be cumbersome for the individuals as well as the health system. The rate of hospitalization can be four times among older people when compared to younger ones. The mean length of hospital stays for AECOPD ranges from 4.5 to 16 days. Moreover there is inadequate protection and less adherence to the treatment due to poor social / family support.

A vast majority of population suffer a sharp decline in the Quality of Life (QoL) after acute exacerbations. A prospective cohort which was followed for six months

showed that only 26% of the patients were both alive and able to report a good, very good, or excellent QoL.

In older people 75% of the episodes of AECOPD, are incited by infections.⁵ Environmental pollution has been implicated in a small proportion of patients up to 10%.⁶ Decrease in air temperature, increased exposure to sunshine, and decreased humidity were also found to be responsible for triggering exacerbations of COPD. The proof that bacterial infections are the causation factors for AECOPD comes from the isolation of pathogens from the lower respiratory tract secretions obtained by different techniques during episodes of exacerbations. The studies which employed bronchoscopy sampling with a protected specimen brush (PSB) to obtain uncontaminated lower airways secretions have found approximately 30% of sputum cultures and 50% of bronchial secretion cultures associated with the presence of potential pathogenic bacteria.^{7,8} Various studies on isolation of pathogens associated with AECOPD suggested that the presence of pathogens was clinically and geographically unpredictable.

In older people comorbidities leads to misdiagnosing and undertreating AECOPD. There is a disparity between practice guidelines and treatment among the older COPD patient. The management of older patients with COPD should encompass a multidisciplinary approach. Along with assessment of the lung ventilator performance and functional impairment, nutritional status and mental health needs to be evaluated.

Definition

GOLD 2018 report defines AECOPD as “an acute worsening of respiratory symptoms that result in additional therapy”.⁹

Exacerbation and concomitant chronic diseases increase symptoms, especially in older people.

Impact

The progression of COPD is associated with increasing frequency and severity of exacerbations. Such exacerbations are associated with short term and long term reductions in quality of life and lung function, as well as increased risk of death^{7,10}. The average patient with COPD experiences two episodes of AECOPD per year, and 10% of these episodes require hospitalization. The average duration of an episode is 7 days, although it may take several months for the patient to return to normal functional status.¹¹

In some patients, exacerbations result in prolonged activity limitation and can quickly reverse the hard-won benefits of exercise training programmes. Exacerbations of COPD have short and long-term clinical implications. The presentations of episodes of exacerbations vary from patient to patient and it depicts the multiple factors involved in the pathophysiology of COPD. Expiratory flow limitation (EFL), as a consequence of airway inflammation, is the pathophysiological hallmark of COPD. The exacerbations in the patients with COPD basically reflect acute worsening of EFL, and there is evidence for both increased airway inflammatory activity and worsening airway obstructions as plausible explanations.¹² It is reasonable to assume that worsening airway inflammation is the primary inciting event of COPD exacerbations and may be caused by bacteria, viruses, or environmental pollutants, including cigarette smoke.

Aetiology of Acute Exacerbations

It is estimated that 70-80% of COPD exacerbations are due to primary respiratory infections, either bacterial or viral. The remaining 20-30% is due to environmental pollution or has an unknown aetiology⁽¹³⁾.

Viral Infection

The most common viruses associated with exacerbations of COPD are rhinoviruses. Influenza, parainfluenza, coronavirus, and adenovirus are also common during exacerbations.¹⁴ Respiratory syncytial virus and human metapneumovirus were more recently associated with exacerbations.^{15,16}

Identification of a virus in the sputum sample of a patient having an exacerbation of COPD does not mean the virus caused the exacerbation. This is supported by the observation that viral nucleic acids can be detected by sensitive PCR-based assays in up to 15% of sputum samples from patients with stable COPD.^{17,18} The pathologic significance of a very low titre infection is uncertain.

The mechanisms by which viruses induce exacerbations have been partially elucidated. Viral infection of the airway epithelial cells induces inflammation.¹⁹ This causes airway epithelial damage, muscarinic receptor stimulation, and induction of inflammatory mediators (eg: cytokines, chemokines). Airway eosinophilia is associated with viral mediated exacerbations, which highlights the importance of the host response to infection and its impact on both inflammation and symptoms.²⁰

Bacterial Infection

Bacterial infections appear to trigger one-third to one-half of COPD exacerbations. *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae* are the bacteria most frequently isolated bronchoscopically from patients with AECOPD.^{21,22} *Pseudomonas aeruginosa* and *Enterobacteriaceae* are also isolated, particularly from patients with severe COPD.

Exacerbations of COPD are strongly associated with acquisition of a new strain of *H. influenzae*, *M. catarrhalis*, *S. pneumoniae*, or *P. aeruginosa*.²³ In one study, exacerbations with a new strain of *Haemophilus influenzae* were significantly more likely to be associated with a humoral immune response than exacerbations with pre-existing strains of *H. influenzae* (61 versus 21 percent).²⁴ The new antibodies were strain specific. *Moraxella catarrhalis* and *Streptococcus pneumoniae* also induce an antibody response that is measurable following an exacerbation of COPD.²⁵ Exacerbations with new bacterial strains are associated with a more robust inflammatory response. Exacerbations of COPD with a new strain of bacteria have been associated with more intense neutrophilic airway inflammation and systemic inflammation than exacerbations with pre-existing bacterial strains or without pathogenic bacteria. Resolution of the airway inflammation is related to eradication of pathogenic bacteria from sputum and resolution of clinical symptoms.

Atypical Bacteria

The incidence of *Chlamydomphila pneumoniae* in exacerbations of COPD appears to be 3 to 5 percent while *Mycoplasma pneumoniae* and *Legionella spp.* are rare.²⁶

Co-Infection

Co-infection appears to increase the severity of COPD exacerbations. In a study of inpatients, Coinfection was associated with a greater decrement of lung function and longer hospitalization.²⁰ In a similar study of outpatients, coinfection was associated with more symptoms, a larger fall in the forced expiratory volume in one second (FEV₁), higher bacterial loads, and systemic inflammation.²⁷

Pathophysiology of Acute Exacerbations

The Expiratory Flow Limitation (EFL) is the pathophysiological hallmark of COPD. Patients with COPD are said to be flow limited when the expiratory flow they generate during tidal respiration represents the maximal possible flow that they can generate at that volume. In flow limited patients the time available for lung emptying (expiratory time) during spontaneous breathing is often insufficient to allow End Expiratory Lung Volume (EELV) to decline to its natural relaxation volume leading to lung over inflation.²⁸

Thus, in flow limited patients, EELV becomes dynamically rather than statically determined, and essentially becomes a continuous variable that fluctuates widely depending on the extent of EFL and the prevailing ventilatory demand. Dynamic hyperinflation (DH) refers to

acute and variable increase in EELV above its baseline value.

DH occurs during exercise in flow limited patients as inspired tidal volume increases and expiratory time decreases, and is associated with severe mechanical constraints on ventilation and perceived respiratory discomfort. DH also occurs during acute bronchoconstriction in asthma. In this setting, the reduction in inspiratory capacity (IC), which reflects the increase in EELV, correlates strongly with the perception of inspiratory difficulty.^{29,30}

During COPD exacerbations airways resistance is abruptly increased (due to bronchospasm, mucosal oedema, and sputum inspissation) and this worsens EFL. The time constant for lung emptying (given by the product of resistance and compliance) is therefore prolonged and EELV is dynamically increased. Furthermore, during an exacerbation, patients tend to adopt a rapid shallow breathing pattern which further limits the time available for lung emptying, thus promoting greater DH in a vicious cycle. In fact, any acute increase in ventilation (such as occurs with anxiety or transient hypoxemia) can be associated with DH in flow limited patients. There is abundant evidence that acute DH may be life threatening during severe exacerbations of asthma or COPD.³¹

However, during COPD exacerbations the mechanical output of the flow limited respiratory system may not increase in proportion to neural drive, resulting in neuromechanical dissociation or uncoupling of the respiratory system. This disparity between central drive and the mechanical response as a consequence of acute DH has been implicated in the genesis of dyspnoea in COPD patients during exercise.³⁰

Clinical Recognition

The symptoms like shortness of breath, cough with expectoration, chest tightness, wheezing are most common symptoms the patients with exacerbations present with. Additional symptoms, such as malaise, body ache, decreased exercise tolerance, fluid retention, increased fatigue and confusion can also be present depending upon the disease severity as well as the extent of physiological derangements.

'Common colds', sore-throat, runny nose, and cough increase significantly during the prodromes, suggesting that respiratory viruses are important exacerbation triggers. The clinical severity of AECOPD varies widely. It may be managed in outpatient setting but may be severe enough to require hospitalizations. When exacerbations are complicated by respiratory failure, intensive care monitoring including ventilatory support, non-invasive or invasive may be required.

Staging of AECOPD

The Winnipeg criteria is derived from a double blind, placebo-controlled trial that evaluated the role of antibiotics in patients with COPD with acute exacerbations.³²

Impact

An acute exacerbation may be mild and require only an unscheduled visit to the physician and outpatient management or may be severe enough to require emergency room, inpatient or even intensive care. AECOPD affects economy, Quality of Life, lung function, physical activity and Central Nervous System functions.

Economic Costs

Hospitalizations during the episode of AECOPD are the main reasons for the use of health care resources and these costs are attributed to the small proportions of patients with repeated exacerbations.³³

Exacerbations account for about 70% of the total costs of COPD management.³⁴

Health related Quality of Life

A vast majority of older people suffer a sharp decline in the Quality of life (QoL) following acute exacerbations. A prospective cohort study which was followed for six months showed that only 26% of the patients were both alive and able to report a good, very good, or excellent QoL.³⁵

Lung function and disease progression

COPD is usually accompanied by a progressive decline in the lung function. The rate of decline in FEV₁ has varied individually considerably both in observational cohorts and intervention trials from 150ml to 200ml per year and few patients may even show increase of up to approximately 159 ml per year. The frequency of exacerbations is one of the determinants of rate of decline.³⁶ Recovery of lung function after an exacerbation is usually less than complete. Smoking and exacerbations have an interactive effect on the progression of COPD, with continued smoking having a worse prognosis.

Physical Activity

AECOPD episode aggravates peripheral muscle weakness. A sharp fall in outdoor activity is seen with exacerbations can lead to a major decline in the time spent outdoors.³⁷ Physical inactivity in turn carries unfavourable prognostic factors which include cardiorespiratory deconditioning which can lead to increase dyspnoea and fatigability, increased risk of venous thromboembolism, worsening of osteoporosis and neuropsychiatric comorbidity.

Neuro-psychiatric Complications

Depression is common complication noted. The ECLIPSE study found a prevalence depression in 26% of patients compared to 12% of controls that increased with disease severity.³⁸ Depression has been a major factor contributing to decreased physical activity, deconditioning and worsening of symptoms, and also adversely impacts adherence, compliance and utilisation of health care.

Treatment Modalities

The management of older people with AECOPD should encompass a multidisciplinary approach. In addition to the assessment of lung ventilatory performance and functional

impairment, nutritional status and mental health should be evaluated. Underlying comorbidities should also be evaluated and treated. Therapy for AECOPD should start with cessation of tobacco smoking.

The goal of treatment is to minimise the negative impact of the current exacerbation and improves Quality of Life.

Beta Agonists and Anticholinergics

Short acting inhaled β_2 agonists and short acting anticholinergics are the initial treatment of COPD exacerbations.^{7,39} At the time of discharge long acting antimuscarinic agonists (LAMA) should be prescribed which has greater effect on exacerbation than long acting β_2 agonists.⁴⁰

Corticosteroids

Systemic corticosteroids have been used as standard treatment for exacerbations for a long time.⁴¹ They have been proved and shown to improve lung function and oxygenation, shorten recovery time and duration of hospitalisation and to reduce treatment failures. The European Respiratory Society (ERS)/ American Thoracic society (ATS) guidelines for the management of COPD exacerbations suggest a short course of 14 days of oral corticosteroids (Prednisolone 1mg/kg) for ambulatory patients with an exacerbation of COPD⁽⁴²⁾. For patients who are admitted to hospitals with acute exacerbations, administration of oral corticosteroids is preferred over intravenous corticosteroids.

Table 1: The WINNIPEG Criteria

Type of AECOPD	Criteria
Type 1	All three of the following symptoms: increase in sputum volume, increase in sputum purulence, Increase in shortness of breath
Type 2	Any two of the following symptoms: increase in sputum volume, increase in sputum purulence, Increase in shortness of breath
Type 3	Any one of the following symptoms: increase in sputum volume, increase in sputum purulence, increase in shortness of breath plus at least one of the following: upper respiratory tract infection lasting for 5 days, fever; increase in wheezes, increase in cough, increase in heart rate >20%

Table 2:

Stopp	Start
<i>Drug prescriptions potentially inappropriate in persons aged > 65 years</i>	<i>Medications for people aged >65 years with the following conditions when no contraindication to prescription exists:</i>
Theophylline as monotherapy for COPD	Regular inhaled beta-2-agonist or anti-cholinergic agent for mild-to-moderate asthma or COPD
Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-to-severe COPD	Regular inhaled corticosteroid for moderate-to-severe asthma or COPD when FEV ₁ is <50% predicted
Nebulised ipratropium with glaucoma	Continuous oxygen at home with documented chronic type 1 or type 2

Antibiotics

Review of all the COPD guidelines revealed that criteria for treatment with antibiotics were mainly an increase in respiratory symptoms.⁴² Studies suggest that antibiotics should only be given in patients with presumed bacterial infection. In order to differentiate between chronic colonisation and acute infection, procalcitonin levels can be assessed as a marker for antibiotic treatment.^{43,44}

Non-invasive Ventilation

A meta-analysis conducted in 2003 concluded that non-invasive ventilation (NIV) is the first line intervention in patients with COPD exacerbation in addition to the usual medical care⁽⁴⁵⁾.

Polypharmacy

The older people having multiple comorbidities will be consuming more than four drugs per day which constitutes polypharmacy. The drugs used for treating exacerbations again add to the list. The drugs which can be stopped temporarily should be discontinued. It also predisposes to the drug - drug interactions.

Inappropriate medications are detected according to various screening tool for the assessment of quality and safety of prescriptions, for example the screening tool of older persons potentially inappropriate prescription (STOPP) and the screening tool to alert doctors to the right treatment, (START).⁴⁶

Inhalation Therapy

Inhaled bronchodilator therapy is the mainstay of treatment in the management of COPD, although it is available in various formulations (metered dose inhaler [pMDI] / dry powder inhaler [DPI] or nebulised), the MDI is the most commonly prescribed.⁴⁷ Therapeutic benefit depends on adequate airway drug deposition. Inhaler technique is crucial, but it is suboptimal in many older patient groups.⁴⁸ Arthritis, poor manual dexterity and visual limitations are potential problems affecting inhaler use.⁴⁹ Nebulisers are frequently used to deliver bronchodilators in older people. Supplemental oxygen for ≥ 15 hrs per day reduces the mortality in patients with COPD.⁵⁰

Nutrition Support

European society for parenteral and enteral nutrition guidelines suggests enteral nutrition in combination with exercise for patients to improve nutritional status and function in patients with COPD.⁵¹

Palliative and end of life care

In advanced stage of COPD, the older people should receive palliative care in order to improve their own and their caregivers quality of life. Palliative care focuses on the prevention and relief of suffering by means of early identification and treatment of all physical, psychosocial and spiritual issues affecting the patient and their relatives.

The palliative care provided within the last 12 months of life is considered as end-of-life care. Smoking cessation and long-term oxygen therapy improve survival as well as quality of life in COPD patients. Non-invasive positive pressure ventilation delivered through nasal or face mask avoids the risk associated with mechanical ventilation and is an alternative to it for symptom relief in end stage COPD.⁵²

Pulmonary Rehabilitation

Pulmonary rehabilitation (PR) plays a very pivotal role in the management of COPD in older people, by breaking the vicious circle of dyspnoea–decreased activity–deconditioning–isolation. PR has been shown to be the most effective non-pharmacological intervention for improving health status and has become a standard of care for patients with COPD.⁵³

Pulmonary rehabilitation is a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies, which include, exercise training, education and behaviour change, designed to improve the physical and emotional condition of people and to promote the long-term adherence of health-enhancing behaviours.⁵⁴

A PR program is not a stand-alone therapy, but rather, should be integrated into a management program. By using a holistic approach individualised on the patient, it aims to reverse the systemic manifestations of COPD as well as to relieve the fears and anxiety associated with social and exterior activities, thereby leading to a change in the patient's day-to-day life.⁵⁵

Therapeutic Compliance

The problems of therapeutic adherence are very frequent in the older people. Compliance to drug therapy in COPD is much lower than that of other common diseases such as diabetes, osteoporosis, and hypertension.⁵⁶

Data from the international literature shows that adherence to treatment in COPD is less than 50% including drug therapy, oxygen therapy and rehabilitation.⁵⁷

The major predictors of poor adherence to medication are presence of psychological problems, presence of cognitive impairment, inadequate follow-up or discharge planning, side effects of medication, patient's lack of belief in benefit of treatment, patient's lack of insight into the illness, poor provider-patient relationship, missed appointment, complexity of treatment, cost of medication.⁵⁸

Comorbidities can affect adherence to therapy because more factors may interfere with drugs assumption (mental impairment, depression, visual impairment, functional limitations related to arthritis, cerebrovascular disease, Parkinsonism). Polypharmacy and device management can also adversely affect compliance.

Conclusion

Acute exacerbations of Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable respiratory disease which is a major cause of chronic morbidity and mortality throughout the world,

The majority of older people suffer a sharp decline in the Quality of life (QoL) after acute exacerbations. The management of older people with COPD should encompass a multidisciplinary approach.

A holistic approach involving Nutritional support, Palliative care, Pulmonary rehabilitation, and End of life care needs to be considered in older People. Immunization against Influenza and Pneumococci prevents exacerbations. World COPD day is observed on 20th November every year.

Conflict of Interest: None.

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