

# Chapter 134

## Management of COPD — A Clinical Scenario

JAISING PHADTARE

### DEFINITION

COPD is characterized by progressive airflow limitation that is not fully reversible and associated with an abnormal inflammatory response of the lungs to noxious substances.

It is considered in an individual having symptoms of chronic cough, sputum production, shortness of breath and history of exposure to risk factors. Diagnosis is confirmed by spirometry (establishing the airflow limitation which is poorly reversible). In situations where spirometry is not available, symptomatology along with prolonged forced expiratory time, a low peak flow is consistent with COPD, though possess poor specificity.

### LIABILITY

- 160 million smokers in India.
- Approximately 14 million Indians are currently suffering from COPD.
- One million Indians die in a year due to smoking related diseases.
- Would be the fifth most prevalent disease by 2020.
- Expected to be the third leading cause of death by 2020.
- It is the only chronic disease that is showing progressive upward trend in both mortality and morbidity.

### CLASSIFICATION

Classification of disease severity into four stages for educational and management purpose is adopted. All  $FEV_1$  values are post-bronchodilator ones. Respiratory failure means  $PaO_2 < 60$  mm Hg (8Kpa) with/without

$PaCO_2 > 50$  mm Hg (6.7 Kpa) while breathing room air. There is no perfect relationship between degree of airflow limitation and symptoms, though treatment of COPD is largely based on symptoms. This approach is aimed at practical implementation.

Stage	Characteristics
0: At risk	Chronic symptoms (cough and sputum production) Normal spirometry
I: Mild COPD	With/without chronic symptoms (cough and sputum production) $FEV_1 \geq 80\%$ of predicted $FEV_1/FVC < 70\%$ mild airflow limitation
II: Moderate COPD	Usually chronic symptoms (cough and sputum production) with shortness of breath developing on exertion $FEV_1$ between 80 to 50% of predicted $FEV_1/FVC < 70\%$ . Worsening airflow limitation
III: Severe COPD	Chronic symptoms (cough and sputum production) with increased shortness of breath and repeated exacerbations $FEV_1$ between 50 and 30% of predicted $FEV_1/FVC < 70\%$ . Further worsening airflow limitation
IV: Very Severe	Chronic symptoms (cough and sputum production) Severe shortness of breath or Chronic respiratory failure Severe airflow limitation ( $FEV_1$ may be 30% or even less)

### CLINICAL FEATURES

- **Chronic cough** – present daily / intermittently, often throughout the day; seldom, only at night time.

- **Chronic sputum production** – any pattern of sputum production, i.e. persistent may indicate COPD.
- **Acute bronchitis** – repeated attacks may lead to COPD.
- **Shortness of breath** – Progressive, persistent, worsening of exercise and during respiratory infection.

Diagnosis of COPD should be based on history of exposure to risk factors, characteristic symptoms of chronic cough, sputum production and/or breathlessness and spirometry.

The diagnosis should be confirmed on spirometry. If not available, then clinical symptoms stated above along with ↑ forced expiratory time (FET) would help. A low peak flow though consistent with COPD has poor specificity.

## INVESTIGATIONS

- **X-ray Chest** – though reveals hardly any diagnostic features, it invariably excludes differential diagnosis like pulmonary tuberculosis.
- **HRCT Thorax** – is also helpful in establishing hyperinflation and emphysematous bullae.
- **Pulmonary Function Test** - obstructive ventilatory defect with bronchodilator reversibility test helps in excluding diagnosis of chronic asthma. Inhaled glucocorticoid (ICS) reversibility test to identify patients having airflow limitations those respond to ICS treatment. Such a test should be performed after a trial of 6 to 12 weeks of ICS. If objective benefit is not achieved, ICS should be discontinued. Diffusion capacity of lung is helpful in establishing diagnosis of emphysema.
- **6-minute walk work** – helps in establishing incapacitating status. It gives an assessment of limitation of activities of daily life to the disease.
- **Arterial Blood Gas Analysis** – Invariably performed in patients having  $FEV_1 < 40\%$  and clinically suggestive of respiratory failure or right heart failure.  $PaO_2 < 60$  mmHg with/without  $PaCO_2 > 45$  mmHg at sea level with room air breathing indicates respiratory failure which may be associated with cyanosis.
- **ECG** – to exclude/detect cardiac involvement.
- **2D Echo** – helps in establishing pulmonary hypertension and also excludes diagnosis of cardiac failure.
- **$\alpha$ -1 Anti-trypsin deficiency** – when COPD develops before 45 years or it develops in patients having

strong family history, the deficiency screening be undertaken.

- **Cadmium level** – interaction between host and environmental exposure to occupational chemicals like cadmium level is vital.

## DIFFERENTIAL DIAGNOSIS

Parameters	COPD	Asthma
<b>Onset</b>	Mid-life	Early in life (often childhood)
<b>Symptoms</b>	Slowly progressive	Vary from day to day and peak in the night/early morning
<b>History</b>	Long smoking history or exposure to smoking and Bio-mass fuel	History of allergy, rhinitis and/or eczema
<b>Inflammatory cells</b>	Neutrophils	Eosinophils
<b>Airway hyper-responsiveness</b>	Poorly reversible	Largely reversible

### • Congestive Heart Failure

In addition to clinical features fine crepitations in both infrascapular regions, chest X-ray showing cardiomegaly, lung functions indicating no airflow limitation but restrictive ventilatory defect are some of the findings noted.

### • Bronchiectasis

Copious purulent expectoration, commonly associated with bacterial infection, presence of gross clubbing, coarse crepitations on auscultation, chest X-ray/HRCT thorax revealing bronchial dilatation and thickened at times, showing gross cystic changes.

### • Tuberculosis

Tuberculosis occurs at any age in addition to the symptoms of chronic cough/expectoration, X-ray chest revealing lung infiltrates or cavitations, microscopic detection of AFB.

## MANAGEMENT

### Principles

- Tobacco smoking (in any form) cessation
- Air pollution control (both indoor & outdoor)
- Relieve symptoms
- Improve exercise tolerance
- Prevent disease progression
- Prevent/treat complications

- Prevent/treat exacerbations
- Reduce mortality
- Prevent/minimize untoward effects of pharmacotherapy

### Plan

- Evaluation and monitoring
- Address risk factors
- Stable COPD and exacerbations
- Hospitalization.

### Evaluation and Monitoring

**Medical history:** A detailed medical history of a new patient known or thought to have COPD should be evaluated:

- Exposure to risk factors
- Past history, including asthma, allergy, sinusitis or nasal polyps, respiratory infections in childhood, and other respiratory diseases
- Family history of COPD or other chronic respiratory disease
- Pattern of symptom development
- History of exacerbations or previous hospitalizations for respiratory disorder
- Presence of comorbidities, such as heart disease and rheumatic disease, that may also contribute to restriction of activity
- Appropriateness of current treatments
- Impact on patient's life, including limitation of activity; missed work days and economic impact; effect on family routines; and feelings of depression or anxiety
- Social and family support available to the patient
- Possibilities for reducing risk factors, especially smoking.

### Addressing Risk Factors

- Tobacco smoking cessation is the single most effective—and cost-effective—way to reduce the risk of developing COPD and stop its progression which can only be achieved with high degree of motivation.
- Progression of many occupationally induced respiratory disorders can be reduced or controlled through a variety of strategies aimed at reducing the burden of inhaled particles and gases.
- Outdoor air pollution – can be achieved by implementing pollution under control legislation on

war footing. Afflicted individuals are advised to stay indoor during pollution episodes and to avoid vigorous exercise outdoor. Wherever available, public announcement of air quality be followed religiously.

- Indoor air pollution – use of smokeless chullas, avoiding ill-ventilation, congestion, overcrowding and stuffing of furniture in the house.

## MANAGEMENT OF STABLE COPD AND EXACERBATIONS

### A. Pharmacotherapy

*Prevents/ improves symptoms, reduces frequency and severity, elevates exercise tolerance as well.*

- **Bronchodilators:** Play a pivotal role. Used to relieve intermittent or worsening symptoms and also on regular basis to prevent/reduce persistent symptoms. Methylxanthines, short – or long acting,  $\beta_2$  agonist, short or long acting and anticholinergics can be administered singly or in combination. Methylxanthines/ $\beta_2$  agonist caused effective bronchial smooth muscle relaxation. Tiotropium bromide is a long acting anticholinergic drug of promise. It has revolutionized management of COPD, acting on M1, M2, M3 receptors, dissociating quickly from M2 and blocking M1, M3 for longer duration of time, has unique action based effects in reduction of cholinergic vagal tone of airways. The drug is safe, easy to administer, with minimal side-effects, good acceptance and affordability being some of the positive features.
- **Glucocorticoids:** It is preferable to administer inhaled glucocorticoids, that too only in patients showing improvement and documented spirometric response and in those having  $FEV_1 < 50\%$  as well as repeated exacebrations. It should be advocated orally or parenterally in all exacerbations. It can be given by nebulization as well. Prolonged treatment may relieve symptoms in appropriate patients, however, does not modify long-term decline in  $FEV_1$  long-term treatment with oral glucocorticoids is not recommended.
- **Vaccines:** Influenza and Pneumococcal vaccines are available. Influenza vaccines reduce serious illness and death in COPD patients by 50%. Given once a year in winter. However, pneumococcal vaccine is recommended once in five years.
- **Mucolytic Agents:** (mucokinetic, mucoregulator): Patients having thick, tenacious sputum could be benefited; otherwise its regular use in stable patients is not recommended.

Drug	Oral	Injectable	Inhaled therapy					
			Nebulization	MDI	Accuhaler / Novolizer	Multi-haler	Diskhaler	Rotahaler
<b>Methylxanthines</b>								
1. Theophylline	+	-	-	-	-	-	-	-
2. Aminophylline	+	+	-	-	-	-	-	-
<b>β<sub>2</sub>-agonist</b>								
1. Salbutamol	+	-	+	+	-	+	+	+
2. Terbutaline	+	+	+	+	-	-	-	-
3. Formeterol	-	-	-	+	+	+	+	+
4. Salmeterol	-	-	-	+	+	+	+	+
<b>Anticholinergics</b>								
1. Ipratropium	-	-	+	+	+	+	+	+
2. Tiotropium	-	-	-	+	+	+	+	+

Drug glucocorticoids	Oral	Injectable	Inhaled therapy					
			Nebulization	MDI	Accuhaler / Novolizer	Multi-haler	Diskhaler	Rotahaler
Methyl-prednisolone	+	+	-	-	-	-	-	-
Prednisolone	+	+	-	-	-	-	-	-
Hydrocortisone	-	+	-	-	-	-	-	-
Beclomethasone	-	-	+	+	-	-	-	-
Budesonide	-	-	+	+	+	+	+	+
Fluticasone	-	-	+	+	+ / -	+	+	+
Mometasone	-	-	-	+	-	+	+	+
Ciclesonide	-	-	-	+	-	+	+	+

- **Anti-tussives:** Regular use contraindicated in stable COPD.
- **Antibiotics:** Only to be used in infectious exacerbations and other bacterial infections.
- **Respiratory Stimulants:** Irrespective of type, regular use is not recommended.

## B. Non-pharmacotherapy

### • Pulmonary Rehabilitation

Reduction in symptoms, improving quality of life and enhanced participation in day-to-day activities are some of the aims of the program.

Exercise training, nutritional counselling and education are the main components. Patients at all stages of disease are benefited from the program. Improvement in exercise tolerance, shortness of breath and fatigue are observed. The benefits are sustained even after a single program of a period of two months. It can

be conducted on in-patient, out-patient basis and even at home.

### • Long-Term Oxygen Therapy (LTOT):

Patients with chronic respiratory failure can be administered oxygen for over fifteen hours per day. It has beneficial impact on pulmonary arterial pressure, polycythemia, exercise capacity, lung mechanics and mental status. Patients belonging to stage III and IV having PaO<sub>2</sub> < 55 mm Hg (7.3 kpa) or SaO<sub>2</sub> of 89% with or without hypercapnea or having PaO<sub>2</sub> between 55 mm Hg (7.3 kpa) and 60 mm Hg (8 kpa) or SaO<sub>2</sub> of 89% with evidence of pulmonary hypertension, peripheral edema suggesting congestive heart failure or polycythemia are incorporated.

### • Surgical Intervention

**Bullectomy:** In carefully selected patients this helps in reducing dyspnea and improving lung functions.

**Lung volume reduction surgery (LVRS):** Removal of the most emphysematous part of the lung to improve ventilation by reduction in hyperinflation and thus enhancing mechanical efficiency of inspiratory muscles has generated considerable interest. Careful selection of patients after initial period of pulmonary rehabilitation is rewarded. Patients with upper lobe emphysema do the best.

## Hospitalization

### Indications

Patients having severe form of background COPD developing new signs like cyanosis, having increase in intensity of symptoms like breathlessness, developing new arrhythmias, showing poor initial response to treatment and having co-morbidities like coronary artery disease, developing new arrhythmias, diagnostic uncertainty, insufficient family support and old age should be admitted.

Persistent risk factors, repeated exacerbations, cor pulmonale, and co-morbidities carry an adverse prognosis and may need ICU admission.

#### Indications for ICU Admission

- Severe dyspnea that responds inadequately to initial emergency therapy.
- Confusion, lethargy, coma.
- Persistent or worsening hypoxemia ( $\text{PaO}_2 < 5.3$  kPa, 40 mm Hg), and/or severe/worsening hypercapnea ( $\text{PaCO}_2 > 8.0$  kPa, 60 mm Hg), and/or severe/worsening respiratory acidosis ( $\text{pH} < 7.25$ ) despite supplemental oxygen and NIPPV.

Assessment of lung functions, ABG analysis, Chest X ray, ECG, other necessary tests to exclude diabetes, poor nutrition, electrolyte imbalance, sputum/blood culture – susceptibility studies should be undertaken and appropriate treatment be executed.

#### Severe Non Life-threatening Exacerbations of COPD

- Assess severity of symptoms, blood gases, chest X-ray.
- Administer controlled oxygen therapy and repeat arterial blood gas measurement after 30 minutes.
- Bronchodilators:
  - Increase doses or frequency.
  - Combine  $\beta_2$ -agonists and anticholinergics.
  - Use spacers or air-driven nebulizers.
  - Consider adding intravenous methylxanthine, if needed.

- Add glucocorticosteroids
  - Oral or intravenous.
- Consider antibiotics
  - When signs of bacterial infection, oral or occasionally intravenous.
- Consider non-invasive mechanical ventilation.
- At all times:
  - Monitor fluid balance and nutrition.
  - Consider subcutaneous heparin.
  - Identify and treat associated conditions (e.g., heart failure, arrhythmias).
  - Closely monitor condition of the patient.

## Non-invasive Mechanical Ventilation

Non-invasive Positive Pressure Ventilation (NIPPV) has been useful to reduce the intubations. It is effective in treating acute respiratory failures.

### Selection criteria

- Moderate-to-severe dyspnea with use of accessory muscles and paradoxical abdominal motion.
- Moderate-to-severe acidosis ( $\text{pH} < 7.35$ ) and hypercapnea ( $\text{PaCO}_2 > 6.0$  kPa, 45 mmHg).
- Respiratory frequency  $> 25$  breaths per minute.

### Exclusion criteria

- Respiratory arrest
- Cardiovascular instability (hypotension, arrhythmias, myocardial infarction).
- Somnolence, impaired mental status, uncooperative patient.
- High aspiration risk; viscous or copious secretions.
- Recent facial or gastroesophageal surgery.
- Craniofacial trauma, fixed nasopharyngeal abnormalities.
- Extreme obesity.

## Invasive Mechanical Ventilation

Patients who show impending acute respiratory failure and those with life-threatening acid-base status abnormalities and/or altered mental status despite aggressive pharmacological therapy are best candidates for invasive mechanical ventilation.

Use of invasive mechanical ventilation in end-stage COPD patients is influenced by likely reversibility of the precipitating event, patient's wishes, and the availability of ICU facilities.

- Severe dyspnea with use of accessory muscles and paradoxical abdominal motion.
- Respiratory frequency > 35 breaths per minute.
- Life-threatening hypoxemia ( $\text{PaO}_2 < 5.3 \text{ kPa}$ , 40 mm Hg or  $\text{PaO}_2/\text{FiO}_2^* < 200$ ).
- Severe acidosis ( $\text{pH} < 7.25$ ) and hypercapnea ( $\text{PaCO}_2 > 8.0 \text{ kPa}$ , 60 mm Hg).
- Respiratory arrest.
- Somnolence, impaired mental status.
- Cardiovascular complications (hypotension, shock, heart failure).
- Other complications (metabolic abnormalities, sepsis, pneumonia, pulmonary embolism, barotrauma, massive pleural effusion).
- NIPPV failure

*Hospital Discharge and follow-up should be decided on the merits of the afflicted.*

### Newer Treatments

Apart from smoking cessation, no treatment shows the progression of COPD. This disease is still associated with active inflammation and progressive proteolytic injury to lung tissue. Suggesting pharmacological intervention. A better understanding of cellular as well as molecular mechanism provides new molecular targets for the development of the drugs.

**Mediator antagonists, Protease inhibitors and Phosphodiesterase 4 inhibitor** are the groups which

would offer effective drug profile in the management of COPD in future.

### SUGGESTED READING

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### Stagewise Management Profile

Stage	0: At Risk	I: Mild	II: Moderate	III: Severe	IV: Very Severe
Characteristics	<ul style="list-style-type: none"> <li>• Chronic symptoms</li> <li>• Exposure to risk factors</li> <li>• Normal spirometry</li> </ul>	<ul style="list-style-type: none"> <li>• FEV1/FVC &lt; 70%</li> <li>• FEV1 ≥ 80%</li> <li>• With or without symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• FEV1/FVC &lt; 70%</li> <li>• 50% ≤ FEV1 &lt; 80%</li> <li>• With or without symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• FEV1/FVC &lt; 70%</li> <li>• 30% ≤ FEV1 &lt; 50%</li> <li>• With or without symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• FEV1/FVC &lt; 70%</li> <li>• FEV1 &lt; 30% or presence of chronic respiratory failure or right heart failure</li> </ul>
	Avoidance of risk factor(s); influenza vaccination				
		Add short-acting bronchodilator when needed			
			Add regular treatment with one or more long-acting bronchodilators		
			Add rehabilitation		
				Add inhaled glucocorticosteroids if repeated exacerbations	
					Add long-term oxygen if chronic respiratory failure. Consider surgical treatments

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