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Seminar

Chronic obstructive pulmonary disease

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Acute exacerbations of underlying COPD are a common cause of respiratory deterioration. Developments have been made in preventive measures, but admission to hospital for acute exacerbations can be expected to remain common. Several expert consensus guidelines have been published to define the appropriate management of COPD patients. These consensus guidelines generally agree, but all acknowledge a lack of large well-controlled clinical studies, especially studies focusing on the management of acute exacerbations. Consequently, many potential controversies exist about the details of managing patients with acute exacerbations. Although studies of many fundamental aspects of management are still needed, the results of controlled clinical trials are sufficient to emphasise the importance of a careful clinical assessment, supplemental oxygen, inhaled bronchodilators to partially improve airway obstruction, corticosteroids to decrease the likelihood of treatment failures and to speed recovery, antibiotics, especially in severe patients, and non-invasive positive-pressure ventilation for treatment of acute ventilatory failure in selected patients.

Chronic obstructive pulmonary disease (COPD) is a major medical problem. In the USA, COPD is the fourth main cause of death. Although established risk factors include occupational exposures and hereditary α_1-antitrypsin deficiency, cigarette smoking is the most important risk factor. Only 15–20% of smokers, however, develop clinically important chronic airflow obstruction;[1] why the proportion is so small is not known, but underlying host factors may play a part.

There has not yet been a precise agreement on a definition of COPD.[2,3] The American Thoracic Society defines COPD as a disease process featuring progressive chronic airflow obstruction due to chronic bronchitis, emphysema, or both.[2] The obstruction to airflow may be partly reversible and some patients may manifest bronchial hyper-responsiveness. Excluded from this definition is asthma, which may also cause chronic airflow obstruction and may be difficult to distinguish from COPD in some cases.[2] Although this definition of COPD well describes common usage, the emphasis on the term chronic bronchitis may not be ideal. Chronic bronchitis is defined clinically by the hypersecretion of mucus, which occurs mainly in large airways, not the site of the progressive chronic airflow obstruction. It has been suggested that a definition of COPD should emphasise the central pathogenic role of an inflammatory process that progressively leads to obstruction by causing fibrosis and distortion of terminal airways, loss of alveolar attachments that tether small airways, hypersecretion of mucus, and contraction of smooth muscle.[4,5] For stable COPD, when the patient is either symptom-free or has symptoms without substantial fluctuation, management should aim to improve the quality of life by relieving symptoms, preventing acute exacerbations, and by slowing progressive deterioration in lung function. Guidelines for comprehensive management of stable COPD have been published.[2,3,6]

Since patients with stable COPD have limited baseline respiratory function, they are at higher risk of developing respiratory failure from respiratory insults, such as pneumonia, congestive heart failure, and pulmonary thromboembolism. There is, however, no widely established definition of acute exacerbations of COPD[2,3,6] among the most common causes of acute respiratory deterioration in patients with COPD. The term acute may indicate any respiratory deterioration due to various causes in underlying COPD. Such a non-specific definition creates difficulties for the interpretation of clinical studies and is not especially helpful to the clinician. We define an acute exacerbation of COPD as an acute tracheobronchitis, generally infectious in aetiology, that occurs in a patient with established COPD. An important element of this definition is that other causes of respiratory deterioration in a patient with COPD such as congestive heart failure, cardiac arrhythmias, pneumothorax, pneumonia, and pulmonary thromboembolism must be excluded.

The exacerbation of COPD is typically manifested by combinations of increased dyspnoea, wheezing, cough, sputum production, and worsened gas exchange. Most patients with exacerbations are managed as outpatients, but admission to hospital is often required for close monitoring and treatment. We focus on the inpatient management of acute exacerbations of COPD.

Prevention of acute exacerbations

The clinical course of COPD is intermittently interrupted by acute exacerbations, especially during the winter months. In one study, 173 patients had a mean of 1·3 exacerbations per year (range 0–9·6).[7] Prevention or attenuation of the severity of exacerbations is an important goal in the management of stable COPD. Education of patients, the stopping of smoking, pulmonary rehabilitation, nutrition, and early medical intervention when symptoms worsen all help to prevent exacerbations. The value of pneumococcal vaccine in COPD is still debatable, but influenza and

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Disorder	Therapy	Strength of recommendation*	Comments
Bacterial infection of airways	Antibiotics	++	Benefits supported by R/PC and R/DB/PC trials,[7,24] especially for severe exacerbations
Airway inflammation	Corticosteroids	+++	Benefits supported by R/DB/PC trials[26†, 30, 31†] may also decrease airway secretions
Bronchoconstriction	Aerosolised-adrenergic agonist	+++	Metered-dose inhaler/spacer equal to wet nebuliser in R/DB trials;[32,33] β-adrenergic agonists may also enhance mucociliary clearance
	Aerosolised ipratopium	+++	Maximum effect same as β-adrenergic agonists but slower onset in R/DB trial[32]
	Combined β-adrenergic agonist +ipratropium	+	Combination therapy more effective than single agents in stable COPD by R/DB/PC trials (see further reading), but no advantage over single agents in acute R/DB trial[33]
	Theophylline+other bronchodilator	··	R/DB/PC trial shows no advantage in adding theophylline to otherwise standard therapy[34†]
Secretions	Stop smoking	+++	By consensus, generally recommended[2,3,6]
	Expectorants, iodides, DNase	··	By consensus, no proven value in acute setting[2,3]
	Hydration in excess of euvolaemia	··	By consensus, no proven value in acute setting[2,3]
	Chest physiotherapy	··	By consensus, no proven value in acute setting; may be useful in select patients[2,3,6,37]
Impaired gas exchange and acute ventilatory failure	Supplemental oxygen (titrated)	+++	By consensus; decreases pulmonary vasoconstriction and improves end-organ function[2,3]
	Treat comorbid disorders that impair gas exchange	+++	By consensus eg, pneumonia, congestive heart failure, pulmonary embolism, pneumothorax[2,3]
	Treat comorbid disorders that impair muscle function	+++	By consensus eg, splinting from rib pain or vertebral fracture, oversedation, malnutrition[2,3]
	Doxapram	+	By consensus[6] possibly useful in selected patients[42†]
	Non-invasive assisted ventilation	+++	Risk of intubation decreased in carefully selected patients[34,35†] (further reading)
	Intubation and mechanical ventilation (when indicated)	+++	By consensus monitor to keep dynamic hyperinflation and auto-PEEP to minimum[2,3,6]

MDI=metered dose inhaler; PEEP=positive end expiratory pressure. ··=not recommended; +=weak recommendation; ++=moderate recommendation; +++=strong recommendation; R=randomised; DB=double-blind; PC=placebo-controlled. *Gradation based on perceived strength of best evidence or by expert consensus. †Specific for patients in hospital.

Treatment of acute exacerbations of COPD

pneumococcal vaccines are recommended and widely used to decrease the frequency of exacerbations. No convincing data support the chronic or intermittent use of prophylactic antibiotics to prevent exacerbations. Chemoprophylaxis with amantadine should, however, be considered for unvaccinated patients during periods of high risk of contracting influenza A infection.[8]

Some additional strategies for prevention of exacerbation are promising, but we cannot present them all. A 6-month trial suggested that inhaled fluticasone may have a role in the long-term treatment of COPD.[9] Future studies are needed to confirm this finding, but patients with exacerbations had moderate to severe exacerbations 86% of the time on placebo but only 60% of the time on inhaled fluticasone. Another approach has been the use of the immunostimulating bacterial extract, OM-85 BV.[10] Patients with stable COPD who were treated with the bacterial extract had the same frequency of exacerbatons as those on placebo but required less than half as many hospital days over the 6-month trial. The risk of being admitted to hospital for a respiratory problem was 30% lower in the group on OM-85 BV than in the group on placebo. The alteration of mucus production also has been used to try to prevent or attenuate exacerbations. A 6-month trial showed that once-daily treatment with a carbocysteine lysine salt significantly decreased the frequency of exacerbations.[11] Carbocysteine is thought to alter mucus production by stimulating sialyl-transferase activity in mucus-secreting cells. Although the drop-out rate for patients was notable, analysis by intention to treat showed that 70% of treated patients were free from exacerbations during the trial compared with 54% of those receiving placebo. Finally, as an antioxidant, N-acetylcysteine may also have prophylactic value in decreasing the frequency of exacerbations.[12]

Assessment

An exacerbation typically includes increased cough, changes in volume, tenacity, and purulence of sputum, and increased breathlessness, wheezing, and chest tightness. In some cases, however, cough may be so ineffective because of severe airway obstruction that increased sputum production is not apparent. In initial assessment of COPD patients with respiratory deterioration, clinicians should look for evidence of comorbid disorders causing or contributing to respiratory deterioraton, and review medications such as sedatives or β-adrenergic antagonists. Finally, acute exacerbations of COPD are only one of many causes of a cough-phlegm syndrome (others include postnasal-drip syndrome, sinusitis, asthma, and gastro-oesophageal-reflux disease), and, therefore, increased cough or sputum production alone in a patient with COPD may not indicate an exacerbation.[13]

History, physical assessment, and arterial blood gases are used to assess the severity of the exacerbation and to judge whether the patient requires admission to hospital. On physical assessment, particular attention should be paid to changes in mental status, use of accessory muscles of respiration, and paradoxical abdominal breathing, since any of these findings suggests respiratory failure. Arterial blood gases are also an important assessment tool, but exact values of arterial partial pressures of oxygen (PO_2) and carbon dioxide (PCO_2) do not define acute respiratory failure since patients with COPD have various baseline values. Instead, changes must be interpreted relative to baseline values and in conjunction with symptoms. Generally, however, an arterial PO_2 of less than 7·3 kPa or a PCO_2 of more than 6·7 kPa with an accompanying acute or acute-on-chronic respiratory acidosis, show acute respiratory failure and are clear indications for admisson to hospital. In the absence of acute respiratory failure, admission to hospital should be judged on ability to manage daily activity at

home, the speed of worsening symptoms or gas exchange abnormalities, response to initial therapy, the patient's home setting, access to follow-up, and the severity of the patient's baseline airway obstruction.[2,3,6] Unlike assessment of asthmatics, the role of spirometry or peak-flow measurements to assess the need for emergency admission to hospital has not been established. Most studies have found a poor correlation between spirometric values alone and successful discharge from the emergency room.[14,15] The potential application of spirometric measurements in the acute setting is an important issue because lack of specific criteria for admission undoubtedly contribute to the fact that at least 17–28% of COPD patients discharged from emergency departments ultimately require admission to hospital.[14,16]

The goals of admission to hospital are to relieve airway obstruction, correct hypoxaemia, and to address any comorbid disorders (eg, congestive heart failure or pneumonia) that may also contribute to respiratory deterioration (table).[2,3,6] Patients with exacerbations are generally medically ready for discharge when they are clinically stable off parenteral therapy for 12–24 h, require inhaled bronchodilators no more than every 4 h, have stable arterial blood gases for 12–24 h, are able to walk at least short distances, and have follow-up arranged. One expert consensus guideline recommends routinely following up peak expiratory flow twice daily in patients staying in hospital to assess progress;[6] however, the clinical value of this approach has not been established and other guidelines do not specifically recommend the practice.[2,3]

Antibiotic therapy

Although non-infectious causes of exacerbations may be important (eg, pollution or inhaled irritants), the major precipitants of exacerbations of COPD are acute airway infections.[17] The infection and consequent inflammatory response by the host leads to increased airway obstruction. At least a third of exacerbations may be caused by viral infections.[18] In one study of 186 patients, rhinoviruses, influenza virus, parainfluenza virus, and coronavirus were significantly associated with acute exacerbations of COPD.[18] Patients did not seem to have increased susceptibility to these viruses, but viral infections did have more serious consequences in COPD patients.

The role of bacteria in precipitating exacerbations is controversial. Bacteria may have a primary role in the development of an exacerbation or represent a secondary superinfection of an initial viral process.[17] The controversy stems partly from the presence of various bacterial species in the airways of 25–50% of patients, even when the COPD is stable.[19,20] A role for bacterial infection has been suggested when there is an abundance of neutrophils in sputum,[7,21] and the fact that bacteria are more often recovereable during acute exacerbations compared with in stable COPD[19] support roles. The major bacterial organisms that have been associated with exacerbations are *Haemophilis influenzae, Streptococcus pneumoniae,* and *Moraxella (Branhamella) catarrhalis.*[19] *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* may play a part.[19,22] Evidence also suggests that during acute exacerbations in patients with a baseline forced expiratory volume in 1 s (FEV_1) of 35% or less predicted, gram-negative bacteria, especially *Enterobacteriaceae* and *Pseudomonas,* spp play an important part in acute exacerbations.[23]

The effects of antibiotics also suggest an aetiological role for bacteria in exacerbations in some patients. A meta-analysis of nine studies showed a small overall benefit with antibiotic treatment for COPD exacerbations.[24] The largest study included 362 exacerbations in 173 outpatients.[7] Compared with placebo, the rate of symptom resolution and improvement of peak expiratory flow during exacerbations was slightly but significantly faster when patients were treated with co-trimoxazole, amoxicillin, or doxycycline. For example, when patients received no antibiotics, mean peak expiratory flow increased from 190 L/min to 210 L/min in 9 days. When these antibiotics were used during exacerbations, the same improvement in peak expiratory flow was seen in only 6 days. More importantly, treatment failures, defined by respiratory deterioration, were nearly twice as likely in the placebo group. Benefit from antibiotics was most evident for patients with the most symptoms (dyspnoea, increased sputum volume, and sputum purulence) and there was a trend in the favour of antibiotics when corticosteroids were used.

Although viral infections probably account for many exacerbations of COPD, bacterial infections do have an aetiological role in some exacerbations in some patients. Many clinicians use antibiotics to treat exacerbations, especially when patients have at least two of increased dyspnoea, increased sputum volume, and sputum purulence.[7] For patients admitted to hospital with acute exacerbations of COPD, the rationale for antibiotic treatment is that: antibiotics are most helpful in patients with the worst symptoms; antibiotics substantially decrease rate of treatment failures when patients have little margin for respiratory deterioration; slightly increaase the rate of recovery; the risks of side-effects from antibiotics are low; and an aetiological role for bacteria in individual cases cannot be excluded. Inexpensive antibiotics, amoxicillin, co-trimoxazole, or doxycycline, are generally selected for treatment of outpatients. If resistant organisms are suspected or when the severity of the patient's clinical condition puts them at high-risk of treatment failure, a second or third generation cephalosporin, fluoroquinolone, newer macrolide, or broad-spectrum penicillin may be preferred.[23,25,26] Studies are needed to select patients who will benefit from antibiotics, show optimum antibiotic choices given local and changing resistance patterns, establish the duration of antibiotic therapy, and test the hypothesis that recurrent infections have a role in progression of COPD.

Anti-inflammatory therapy

The acute inflammatory response to infections of the airways stimulates mucus hypersecretion, airway-wall oedema, and smooth-muscle contraction. Abundant neutrophils in sputum suggests a primary or secondary bacterial infection.[21] One study has shown that sputum sampled during acute exacerbations typically had a greater increase in eosinophils than neutrophils, and bronchial biopdies showed substantial airway eosinophilia with a small increase in neutrophils and activated T lymphocytes.[27] Although there is always the question of how well asthmatics are excluded from a

study such as this, the eosinophilic inflammation seemed to be different from that seen in asthmatics since expression of interleukin 5 was not seen during exacerbations of COPD.[5]

Theoretically, corticosteroids could decrease such airway inflammation in COPD. One study showed that severely obstructed patients treated with intravenous methylprednisolone had more rapid improvement of FEV_1 over the first 72 h of a stay in hospital than patients not given corticosteroids.[28] The absolute differences between the groups were small, with increases in FEV_1 of about 0·240 mL in the methylprednisolone group and only 0·135 mL in the placebo group. The study did show, however, that 12 of 22 patients who received methylprednisolone had more than a 40% improvement in FEV_1 after 72 h, but only three out of 21 patients on placebo had similar improvements. Another study of 27 outpatients assessed the effects of corticosteroids on exacerbations of COPD and found that corticosteroids slightly increased the rate of improvement in oxygenation and spirometry and decreased the treatment failure rate.[29] Of those 14 patients treated with placebo, eight had no improvement in symptoms or required admission to hospital. For patients treated with prednisolone, none of 13 had treatment failure. A different study of 30 patients suggested that corticosteroids significantly decreased the rate of relapse from 33·3% to 8·9% in the first 48 h after discharge from the emergency department.[30] Finally, data from the Systemic Corticosteroids in COPD Exacerbations clinical trial support the use of corticosteroids in patients admitted to hospital for acute exacerbations of COPD.[31] In that trial, patients treated with systemic corticosteroids had fewer treatment failures, better spirometry, and shorter hospital stays. Based on all such evidence, patients admitted to hospital for COPD exacerbations commonly receive systemic corticosteroids. The rationale is that although the favourable effect of corticosteroids is modest, even a small improvement is beneficial in patients with severe airway obstruction who cannot tolerate further respiratory deterioration. Additional studies are needed to find the optimum dose and duration of corticosteroid therapy during acute exacerbations. Importantly, the resolution of an acute exacerbation after corticosteroids for 7–14 days should not be taken as an indication for chronic systemic-corticosteroid therapy.

Bronchodilator therapy

Obstruction to airflow results in increased respiratory work, hyperinflation that places the respiratory muscles at mechanical disadvantage, and impaired ventilation-perfusion matching that causes hypoxaemia. Therefore, relief from airflow obstruction to prevent or correct respiratory failure is a major goal in the treatment of acute exacerbations.

Relief from bronchoconstriction is the most rapid means of improving airway resistance, and the improved airflow may help to make cough more effective in clearing secretions. Unfortunately, bronchoconstriction is generally not the only or major cause of airway obstruction during an exacerbation of COPD, and, therefore, the immediate effects of bronchodilation are often only slight. Small improvements in airfow may, however, benefit patients with severe airflow obstruction; therefore, rapidly acting β-2-adrenergic agonists delivered by aerosol are the mainstay of initial treatment. In one typical study, inhaled orciprenaline increased the FEV_1 from about 0·69 L to 0·93 L in 30–60 min.[32] Evidence suggests that metered-dose inhalers with spacers are as effective as wet nebulisation for delivery of β-adrenergic agonists.[33]

Ipratropium bromide, an anticholinergic delivered by inhalation, has been used to treat acute exacerbations. As a single agent, the effects of ipratropium on spirometry are at least equal to the slight effects of β-adrenergic agonists, possibly with less risk of decreased blood oxygenation. Patients with exacerbations of COPD on inhaled ipratropium had a small but significant increase (0·8 kPa) in arterial PO_2 within 30 min. By contrast, with inhaled metaproterenol there was a transient decrease (0·8 kPa) in arterial PO_2.[32] This decrease in arterial PO_2 after β-adrenergic agonists has been attributed to transient worsening of ventilation-perfusion matching because of vasodilation of the pulmonary vasculature, or increases in cardiac output, or both. Since the rate of onset for bronchodilation is slow with ipratropium (peak effect 60–90 min), many physicians prefer β-adrenergic agonists as the first-line bronchodilator during acute exacerbations. In practice, β-adrenergic agonists and ipratropium are frequently combined to treat exacerbations, especially when patients respond poorly to therapy. Extrapolation from studies of patients with stable COPD support combination therapy, but at least one study of acute exacerbations did not show any benefit from the combination of these agents.[32]

The roles of the bronchodilators theophylline or intravenous aminophylline have diminished because of toxic effects and little proof of efficacy when combined with other bronchodilators. One study showed that aminophylline added no benefit to standard treatment of acute exacerbations of COPD.[34] Another showed a non-significant trend in favour of aminophylline.[35] The drug is now used mainly if inhalational agents cannot be given.

Clearance of secretions

After airways are opened and the inflammatory response that promotes mucus hypersecretion and bronchoconstriction has decreased, bronchodilators, antibiotics, and cortiosteroids all help to relieve airway obstruction by decreasing tracheobronchial secretions. Additionally, β-adrenergic agonists may stimulate mucociliary clearance.[36] Besides the pharmacological measures, cigarette smoking should be stopped because the irritant effects of smoke may stimulate mucus secretion, promote airway inflammation, and impair mucociliary clearance. The teaching of "huff coughing" may help patients to clear secretions.[2] Other measures to improve clearance of mucus during exacerbations (eg, expectorants and mucolytics such as N-acetylcysteine, iodides, guaifenesin, and DNase) have limited proven value.[2,3] Unless more than 25 mL of sputum is produced per day or there is mucus plugging with lobar atelectasis, chest physiotherapy has no proven value during exacerbations.[2,37] Nasotracheal suctioning has been used to help some patients clear secretions but the technique has serious risks, and we believe that safer alternatives should be used.[38] Similarly, bland aerosol therapy, and systemic hydration in excess of euvolaemia have no proven role in the treatment of COPD.

Supplemental oxygen therapy

During exacerbations, hypoxaemia is caused mainly by worsened ventilation-perfusion matching. As airway obstruction becomes more severe and the duration lengthens, respiratory muscles may be unable to sustain breathing. Alveolar hypoventilation contributes to further hypoxaemia, hypercarbia, and respiratory acidosis. Hypoxaemia and respiratory acidosis promote pulmonary vasoconstriction that, in turn, causes high pulmonary-artery pressures, which imposes an added load on the right ventricle of the heart. When right-ventricular failure complicates exacerbations of COPD, supplemental oxygen, diuretics, but not digitalis, can improve function. Severe hypoxaemia and hypercarbia with respiratory acidosis may also compromise left-ventricular function, precipitate arrhythmias, impair respiratory muscles, and depress mental status.

Correction of hypoxaemia to achieve an arterial oxygen tension of at least 7·3–8·0 kPa is the immediate priority of management of patients admitted to hospital for acute exacerbations of COPD and specific recommendations for stepwise controlled correction of hypoxaemia have been made in guidelines.[2,3,6] In many cases, low-flow oxygen administered by nasal prongs (1–2 L/min) or venturi-type facial masks (28%) is sufficient. Administration of oxygen is carefully controlled and arterial blood gases are serially monitored because, in a few patients, arterial PCO_2 may increase and an acute respiratory acidosis occur. Patients developing an arterial pH of less than 7·26 when supplemental oxygen is delivered have a significantly poorer outlook.[39] The mechanism underlying the acute increase in arterial PCO_2 that occurs in some patients is not clear. Emphasis has previously been placed incorrectly on supplemental oxygen therapy causing hypercapnia because of depressed hypoxic drive to breathe in patients with COPD. Most evidence now suggests that minute ventilation and drive to breathe do not decrease with supplemental oxygen.[40] The rise in arterial PCO_2 after administration of supplemental oxygen, is probably due to the Haldane effect and worsening ventilation-perfusion matching.

Assisted ventilation

Neuromuscular function may be unable to meet or sustain the increased work of breathing imposed by increased obstruction to airflow. Impaired neuromuscular function by depressed consciousness and fatigue or weakness of respiratory muscles can contribute to acute ventilatory failure during exacerbations of COPD.[41] Therefore, correction of factors that impair respiratory neuromuscular function is important, such as electrolyte disturbances, pain-causing splinting, abdominal distension or ascites, poor nutrition, and any sedating drugs that are contraindicated unless the patient is receiving assisted ventilation. The use of the respiratory-muscle stimulant doxapram to increase alveolar ventilation in acute ventilatory failure may be beneficial. In one study, half as many patients treated with doxapram had increases in PCO_2 during the first 2 h after admission to hospital.[42] No study has shown that doxapram decreases the need for assisted ventilation and use of this medication to treat patients with acute ventilatory failure has not been widely adopted.

Despite maximum medical therapy, some patients with exacerbations of COPD will have severe and progressive acute respiratory acidosis, severe hypoxaemia, or both, despite supplemental oxygen. Assisted ventilation provides short-term support while airway obstruction is treated. Evidence indicates that non-invasive positive-pressure assisted ventilation is useful for severely ill patients who do not require immediate endotracheal intubation.[43–45] Mechanical ventilation, with its potential complications of barotrauma and infection, can then be avoided. The best time to start non-invasive mechanical ventilation is not established, but early intervention if the respiratory rate is more than 30 breaths per min and the pH is less than 7·35 has been suggested.[46] Successful non-invasive positive-pressure assisted ventilation should improve respiratory rate and pH within 1 h. Positive pressure via a tight-fitting facial or nasal mask lessens the work of breathing, which may allow recovery of fatigued respiratory muscles. Interestingly, even brief periods (6–8 h/day) of non-invasive support seem to decrease the risk of an eventual need for intubation.[44] This technique is recommended only for tolerant and cooperative patients who are not sedated, are haemodynamically stable, able to protect their airways and clear secretions, and, importantly, are cared for by intensive-care support staff familiar with non-invasive support. This technique will probably become an increasingly popular short-term intervention for select patients.

General guidelines for endotracheal intubation during acute exacerbations of COPD

Persistent hypoxaemia with failure to reach arterial PO_2 55–60 mm Hg or O_2 saturation <88–90% despite maximum therapy, including supplemental oxygen
Worsening acute respiratory acidosis despite maximum therapy
Signs of progressing respiratory-muscle fatigue despite maximum therapy
Deterioration of mental status
Inability to protect airway
Inability to clear copious secretions

The decision to intubate and initiate mechanical ventilation is complex; each patient's baseline quality of life is an important consideration (panel). Notably, the absolute value of arterial PCO_2 alone should not be used to indicate the need for intubation since many patients with severe COPD may have a baseline compensated respiratory acidosis and do not require assisted ventilation. Arterial PCO_2 must be assessed in relation to arterial pH. When patients do require intubation and mechanical ventilation for exacerbations, they should be supported with positive-pressure ventilation with assist-control, intermittent-mandatory, or pressure-support, ventilatory methods. Pressure-support ventilation may be more comfortable for patients but outcomes have not been shown to be different from the two other methods. The major complications of invasive positive-pressure ventilation are barotrauma, pneumonia, and local complications of endotracheal tubes. Risk of barotrauma is decreased by keeping the autopositive end-expiratory pressure to a minimum.[2,3]

General management

We practise the following general-management plan. For inpatient treatment of acute exacerbations of COPD, assessment begins with clinical assessment and measurement of arterial blood gases for evidence of respiratory failure that needs assisted ventilation. We

identify comorbid illnesses, such as pneumonia, and medications that could contribute to respiratory deterioration. Various treatments are started. Controlled low-flow, supplemental oxygen is delivered to achieve and maintain an arterial PO_2 of at least 7·3–8·0 kPa. Delivery of oxygen by nasal prongs is generally preferred to mask delivery because prongs are more comfortable and patients are more likely to leave them in place. Arterial blood gases are measured serially when patients are on supplemental oxygen to ensure that they are not among the minority who develop respiratory acidosis upon delivery of oxygen. We administer a broad-spectrum antibiotic. For patients admitted to hospital with severe airflow obstruction at high risk of treatment failure, we generally select a second-generation cephalosporin, fluoroquinolone, or second-generation macrolide. Bronchospasm is treated and mucociliary clearance possibly improved with inhaled β-adrenergic agonists, given by metered-dose inhaler and spacer under direct supervision. For patients with severe or rapidly progressive deterioration and only a slight response to β-adrenergic agonists, ipratropium by inhalation every 4–6 h is added. Patients are started on intravenous methylprednisolone and changed to prednisolone after 1–3 days when clear improvement is seen. To help mobilise secretions, patients are encouraged to cough while sitting upright in a chair, and early ambulation is encouraged. Chest physiotherapy is not done routinely since evidence is insufficient to show any value in acute exacerbations. Throughout treatment, patients undergo frequent clinical assessments, and arterial blood gases and oximetry are monitored to assess response to therapy. For patients who have severe and worsening symptoms of respiratory acidosis despite therapy, or who have hypoxaemia on supplemental oxygen, assisted ventilation is used (panel). For select patients, non-invasive ventilation is preferred.

Any general approach to acute exacerbations of COPD must acknowledge the lack of large, double-blind, placebo-controlled clinical trials addressing fundamental questions of management. Comprehensive, widely accepted, evidenced-based guidelines for management do not yet exist. Expert consensus guidelines do, however, agree on many issues.[2,3,6]

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