Acute severe asthma

Acute severe asthma is a medical emergency associated with a significant morbidity and mortality. Many of the adverse outcomes are attributed to underestimation of severity with delayed and/or inadequate treatment and are potentially preventable. Although the prevalence of asthma is increasing, many countries have achieved reductions hospital presentations and admissions, reduced intensive care admissions and reduced overall asthma mortality.

CLINICAL DEFINITION

Asthma has been defined as a lung disease with the following characteristics:

(i) airway obstruction that is reversible (completely or partially) either spontaneously or with treatment,
(ii) airway inflammation, and
(iii) increased airway responsiveness to a variety of stimuli.

Exacerbations of asthma are characterized by increasing dyspnea, cough, wheeze, chest tightness and decreased expiratory air flow.

Status asthmaticus

has had varying definitions. However, for practical purposes, any patient not responding to initial doses of nebulized bronchodilators should be considered to have status asthmaticus.

AETIOLOGY:

The pathogenesis of asthma is complex with both genetic and environmental influences. The increase in asthma prevalence has been attributed to the 'hygiene hypothesis', which suggests that reduced exposure to childhood infections as a result of antibiotics and hygienic lifestyle promotes an imbalance in T-cell phenotype leading to inflammatory cytokine overproduction. IgE-dependent mechanisms appear to be particularly important in generating the characteristic state of airway

inflammation and bronchial hyperreactivity with the allergens in the local environment dictating the specificity of the antibody response.

Triggers of acute asthma can be

- non-specific (cold air, exercise, atmospheric pollutants),
- specific allergens (housemite, pollen, animal danders),
- modifiers of airway control (aspirin, beta blockers), or
- stress or emotion.

No precipitant can be identified in over 30% of patients.

PATHOPHYSIOLOGY

The post-mortem airway pathology of patients who die from acute asthma includes bronchial wall thickening from oedema and inflammatory cell infiltrate, hypertrophy and hyperplasia of bronchial smooth muscle and submucosal glands, deposition of collagen beneath the epithelial basement membrane and prominent intraluminal secretions. These secretions may narrow or occlude the small airways.

Physical examination

The general appearance and level of distress can be an important indicator of severity (Table 35.1).

- Use of accessory muscles,
- suprasternal retraction,
- markedly diminished breath sounds or a silent chest,
- central cyanosis,
- inability to speak,
- a disturbance in the level of consciousness,
- upright posture and
- diaphoresis

  all suggest a severe attack.

- A respiratory rate >30/min,
- pulse rate >120/min and

- pulsus paradoxus of >15 mmHg (2 kPa) is associated with severe asthma though their absence does not preclude life-threatening asthma.
- Patients with diminished perception of dyspnea may mask severe asthma and lead to underestimation of severity. Ventilatory function tests the patient may not be able to perform these due to breathlessness. However, FEV1 and peak expiratory flow rate (PEFR) are useful indicators of severity and response to treatment when done serially.

Table 35.1 Assessment of asthma severity

	MILD	MODERATE	SEVERE
Conscious state	Alert, relaxed	Anxious, difficulty sleeping	Agitated, delirious
Speech	Sentences	Phrases	Words
Accessory muscles	Nil	Mild	Significant sitting upright
Wheeze	Moderate	Loud	Loud or silent
Pulse rate (BPM)	<100	100–120	>120
Peak expiratory flow (% predicted)	>80%	60–80%	<60%
Pa_{CO_2} (mmHg) (kPa)	<45 (5.98)	<45 (5.98)	>45 (5.98)

MANAGEMENT

ESTABLISHED TREATMENTS

Initial therapy of acute severe asthma should include the following:

➢ OXYGEN

Hypoxemia contributes to life-threatening events that complicate acute severe asthma. Humidified supplemental oxygen should be titrated to achieve a SpO2 >90%.

➢ BETA AGONISTS

Short-acting beta agonists remain the first-line bronchodilator therapy of choice. Agents include salbutamol (albuterol), terbutaline, isoproterenol (isoprenaline) and epinephrine (adrenaline). Salbutamol is generally the agent of first choice as it has relative β2- selectivity, with decreased β1-mediated cardiac toxicity.

Long-acting beta agonists such as salmeterol have no role in status asthmaticus owing to slow onset of action and association with fatalities in this setting. Beta agonists cause bronchodilatation by stimulation of β2-receptors on airway smooth muscle and may reduce bronchial mucosal oedema.

➢ ANTICHOLINERGICS

Anticholinergics cause bronchodilatation by decreasing parasympathetic-mediated cholinergic broncho motor tone. Ipratropium bromide is the most commonly used anticholinergic for asthma and is a quaternary derivative of atropine. Ipratropium is now widely used as first-line therapy for acute severe asthma in conjunction with beta-agonist therapy.

➢ CORTICOSTEROIDS

The role of corticosteroids in the acute asthma attack has been well established. Systemic steroids should be considered in all but mild exacerbations of asthma. Their benefits include increased β-responsiveness of airway smooth muscle, decreased inflammatory cell response and decreased mucus secretion. Side-effects of corticosteroids include hyperglycemia, hypokalemia, hypertension, acute psychosis and myopathy, though they are usually well tolerated acutely.

➢ AMINOPHYLLINE

There have been conflicting reports regarding the efficacy of aminophylline in acute asthma ranging from no benefit to improved lung function and improved outcome. However, it is accepted that aminophylline is an inferior bronchodilator, with a narrow therapeutic range and frequent side-effects including headache, nausea, vomiting and restlessness, with cardiac arrhythmias.

NON-ESTABLISHED TREATMENTS

A number of other therapies have reported benefit in acute severe asthma, but their role in addition to full standard therapy has not been clearly established and they are not advocated for routine use.

However, these modes of therapy can be considered in the patient who is in extremis or remaining severe despite conventional treatment.

➢ EPINEPHRINE

Epinephrine has some theoretical advantages over pure β2-agonists in that its additional α-agonist actions of vasoconstriction and mucosal shrinkage may improve airway caliber.

➢ MAGNESIUM SULPHATE

Magnesium sulphate is postulated to block calcium channels, and possibly acetylcholine release at the neuromuscular junction, leading to smooth muscle relaxation and bronchodilatation.

➢ HELIOX

Inhalation of a helium: oxygen mixture reduces gas density and turbulence with reduced air-flow resistance. The most effective gas mixture is 70% helium (30% oxygen) and the minimum concentration likely to provide benefit is 60% helium.

➢ ANAESTHETIC AGENTS

Ketamine, a dissociative anesthetic agent, has been used in severe asthma. It may cause bronchodilatation by both sympathomimetic potentiation and a direct effect on airway smooth muscle. Ketamine may be

a useful induction agent for endotracheal intubation (dose 1–2 mg/kg) as it may ameliorate the bronchoconstrictor response to intubation.

➢ LEUKOTRIENE ANTAGONISTS

Leukotriene antagonists have shown benefit in chronic asthma and there is some evidence of benefit in acute asthma.

➢ BRONCHOALVEOLAR LAVAGE

Bronchoalveolar lavage has been used in severe refractory asthma to clear mucous plugging during mechanical ventilation. It can transiently worsen bronchospasm and hypoxemia and should be used when air-flow obstruction has stabilized.

VENTILATION IN ASTHMA

DYNAMIC HYPERINFLATION

In all degrees of air-flow obstruction, slow expiratory air flow results in incomplete exhalation of gas during normal expiratory times. Gas is trapped in the lungs by the arrival of the next breath and the lungs are unable to return their normal passive relaxation volume (functional residual capacity, FRC). Incomplete exhalation of each successive breath causes progressive accumulation of trapped gas called dynamic hyperinflation (DHI).

NON-INVASIVE VENTILATION (NIV)

Non-invasive ventilation (NIV) has been widely used for a variety of respiratory problems. In severe asthma there are a number of potential benefits. Externally applied PEEP may help overcome PEEPi due to gas trapping and thus reduce the inspiratory threshold work of breathing. Augmentation of inspiration with NIV may further decrease the work of inspiration and increase tidal volume and minute ventilation. If tidal volume is increased with a shorter inspiratory time, then increased minute ventilation can occur without a proportional increase in dynamic hyperinflation. Both inspiratory augmentation and PEEP may facilitate airspace opening, thus reducing V/Q mismatch.

Indications for use are:

- moderate to severe dyspnea or respiratory distress,
- hypercapnic acidosis, and
- respiratory rate >25, accessory muscle use or paradoxical breathing.

Contraindications to NIV

- cardiac or respiratory arrest,
- a decreased conscious state,
- severe upper gastrointestinal bleeding,
- hemodynamic instability,
- facial trauma or surgery,
- inability to protect the airway and clear secretions and high risk of aspiration.

Nasal masks are usually not suitable in acute respiratory failure and facemasks of full-face masks fitted to achieve comfort and a reliable seal are usually best. NIV should be commenced with 5 cmH2O CPAP (expiratory positive airway pressure, EPAP 5 cmH2O) and 8–10 cmH2O pressure support (inspiratory positive airway pressure IPAP 13–15 cmH2O).

Complications of NIV

- nasal bridge ulceration,
- mask discomfort,
- nasal congestion,
- gastric insufflation,
- aspiration,
- hypotension and
- pneumothorax.

INVASIVE VENTILATION

Invasive mechanical ventilation in acute severe asthma may be lifesaving but can be associated with significant morbidity and mortality. Institution of invasive ventilation with endotracheal intubation carries the risk of inadvertent pulmonary hyperinflation and potential aggravation of

bronchospasm and a significant part of the morbidity and mortality has been attributed to pulmonary hyperinflation. Despite these risks, the incidence of mechanical ventilation for asthma is decreasing and mortality of patient ventilated for asthma is also decreasing in some series. The decision to intubate depends on both the clinical status of the patient and the natural history of the type of asthma present. Hyperacute asthma may present with marked hypercapnia ($PaCO_2 > 60$ mmHg (7.98 kPa)) due to mechanical limitations of ventilation as a result of dynamic hyperinflation. Such patients may not initially be fatigued and may respond rapidly to treatment, thereby avoiding mechanical ventilation.

Acute severe asthma that has been progressing for days may have less hypercapnia but will often respond poorly to treatment. The $PaCO_2$ may rise despite maximal treatment owing to fatigue and the patient may require intubation at a lower $PaCO_2$. The general principles are to use NIV early but to avoid mechanical ventilation if safe to do so. The decision to intubate is based primarily on the degree of respiratory distress as assessed by an experienced clinician and the patient themselves.

Absolute indications for intubation

- cardiac or respiratory arrest,
- severe hypoxia or rapid deterioration of conscious state.

Once the decision to intubate has been made, a safe option is to perform rapid sequence intubation using the orotracheal approach. A large as possible endotracheal tube should be used to reduce the work of breathing and to reduce the risk of tube occlusion by the tenacious secretions that often occur with asthma. Once the endotracheal tube is in place, slow hand ventilation (8–10 breaths/minute) should maintain oxygenation until the ventilator can be connected.

INITIAL VENTILATOR SETTINGS

The principles of initial mechanical ventilation are avoided excessive DHI and to avoid excessive hypoventilation by commencing with a minute ventilation <115ml/kg/min best achieved with

- a tidal volume of 5–7 mL/kg,
- a respiratory rate of 10–12 breaths/min and
- a short inspiratory time to ensure an expiratory time ≥4 seconds.

This degree of hypoventilation will usually result in hypercapnic acidosis and continued respiratory distress necessitating heavy sedation, and sometimes requires 1–2 bolus doses of a neuromuscular-blocking agent.

The use of volume-controlled ventilation is most established for this ventilatory pattern. In volume control, a high inspiratory flow rate (70– 100 L/min) is required to achieve a short inspiratory time. This will result in a high peak airway pressure (PIP) but this will lower DHI and Pplat and reduce barotrauma compared with lower inspiratory flow rates.

MCQ TEST

1- Characteristics of asthma (all true except one)
   a) airway obstruction that is reversible
   b) airway inflammation
   c) increased airway responsiveness to a variety of stimuli
   d) Exacerbations of asthma are characterized by increasing dyspnea, cough, and wheeze
   e) Not occur in pediatrics
2- Complications of noninvasive ventilation in asthma (all true except one)
   a) nasal bridge ulceration,
   b) gastric insufflation,
   c) aspiration
   d) hypertension
   e) pneumothorax.
3- Contraindications of NIV in asthma (all true except one)

a) cardiac or respiratory arrest,
b) decreased conscious state,
c) hypotension
d) hypercapnic acidosis
e) inability to protect the airway and clear secretions and high risk of aspiration.

4- the first-line bronchodilator therapy for asthmatic patient is
a) salbutamol
b) Terbutaline
c) isoproterenol
d) epinephrine
e) norepinephrine

5- trigger factors for acute asthma (all true except one)
a) cold air
b) exercise
c) Aspirin
d) propranolol
e) Corticosteroid

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