Use of mechanical ventilation in adults with severe asthma

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Asthma severe enough to require intubation and mechanical ventilation is associated with a mortality rate of about 10%. Therapeutic modalities are ever-changing and at times controversial. This paper provides an update on such modalities and presents, in a step-wise fashion, those most appropriate for practical patient care. The timing of intubation and the methods used to control airway patency, arterial pH and gas levels, and hemodynamic status are crucial to the success of therapy. Finally, conventional and disputed methods of bronchodilation are outlined.

Un taux de mortalité d'environ 10% est rattaché à l'asthme lorsque celui-ci est assez grave pour nécessiter intubation et ventilation mécanique. Les modalités de traitement changent continuellement et font parfois l'objet de controverse. Cet article fait le point sur les dernières modalités thérapeutiques et présente, étape par étape, celles qui sont les plus appropriées en matière de soins pratiques aux malades. Le moment choisi pour l'intubation, et les méthodes utilisées pour vérifier la liberté des voies respiratoires, le niveau du pH et des gaz artériels ainsi que l'état hémodynamique sont cruciaux pour le succès d'un traitement. Finalement, on expose les grandes lignes des méthodes conventionnelles ou contestées de bronchodilatation.

There have been many reviews of asthma therapy that have discussed immunotherapy, bronchodilating agents and the avoidance of precipitating factors. However, comparatively little has been written on the difficult and controversial management of an asthmatic patient in respiratory failure who requires intubation and intermittent positive pressure ventilation (IPPV). The high and labile airway resistance in such patients necessitates a different approach than is used in those with predominantly chronic bronchitis or emphysema and a small amount of reversible airway obstruction. The mortality rate among patients with asthma who require IPPV is approximately 10%. However, it has been found to range from over 30% in older studies to 0% in some recent studies, presumably reflecting improvements in management.[1,2]

We will discuss how to determine whether a patient with acute asthma requires IPPV and will offer a practical, stepwise approach to management once the decision to mechanically ventilate has been made.

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Indications for IPPV

In patients with severe asthma, IPPV should be instituted when the risks of intubation and mechanical ventilation are judged to be less than those of continued conservative management. Our experience and a review of the current literature have provided guidelines for deciding whether to use mechanical ventilation. Frequent re-evaluation may be necessary, as the condition of patients with mild arterial blood-gas abnormalities may deteriorate quickly, whereas those with poor gas exchange may be alert and subsequently improve.[3]

The indications for IPPV are listed in Table I. However, no one factor is an absolute indication for IPPV. During an acute asthma attack the arterial carbon dioxide pressure ($PaCO_2$) usually decreases owing to hyperventilation. However, when it increases to 40 mm Hg and there is no evidence of improvement the patient should be monitored closely in an intensive care facility, where an intra-arterial line can be inserted and prompt resuscitation is available. Although an elevated $PaCO_2$ is an ominous sign, correlating with a forced expiratory volume in 1 second (FEV_1) of less than 25%, Bondi and Williams[8] found that of 27 asthmatic patients whose $PaCO_2$ was greater than 40 mm Hg at the time of admission 23 did not require intubation. The average $PaCO_2$ was 75 mm Hg in the patients who required ventilation, compared with 55 mm Hg in those who did not, but there was considerable overlap in the values.

It must be remembered that patients who require ventilation are often young, may never have been admitted to hospital before and are terrified. Repeated reassurance and explanations, especially regarding intubation, sedation and paralysis, are essential to alleviate fear and enhance cooperation.

Management with IPPV (Table II)

Intubation

Intubation of a patient with acute asthma entails considerable risk. Stimulation of the larynx and trachea may reflexively increase the bronchospasm, thereby aggravating the already severe hypoxemia and acidosis. The increase in airflow resistance may make subsequent venti-

Table I—Indications for intubation and mechanical ventilation

Clinical findings*
Diminished level of consciousness[4]
Diminished response to pain[4]
Progressive exhaustion[5]
Absent breath sounds and wheezing[6]
Fixed chest[6]
Pulsus paradoxus[7]
Arterial blood gas levels
pH less than 7.2
Carbon dioxide pressure
Increasing by more than 5 mm Hg/h[6]
Greater than 55 to 70 mm Hg
Oxygen pressure less than 60 mm Hg[6]
Evidence on chest x-ray films
Pneumothorax[7]
Pneumomediastinum[7]
Results of spirometric tests
Forced expiratory volume in 1 second less than 500 mL or vital capacity less than 1000 mL and failing to improve with bronchodilators[7]

***Combined with decreasing arterial blood gas levels.**

lation extremely difficult. The procedure should therefore be performed by an experienced physician. The patient's blood pressure and cardiac rhythm must be monitored.

Although many premedication regimens are used, there are no published data that suggest which is best. However, in an alert patient the pharynx and larynx must be thoroughly anesthetized with lidocaine to minimize discomfort and inhibit bronchospasm. Thereafter, fast-acting sedatives with or without paralytic agents may be given immediately before intubation according to the patient's needs and depending on the premedication regimen with which the physician is most experienced.

One of us (P.W.M.) has found that the use of halothane simplifies intubation and is useful in the initial control of ventilation. Halothane is fast acting, it does not irritate the larynx, and its effect can be controlled. By dilating the bronchial smooth muscle it improves airflow, and by relaxing the skeletal muscles of the chest wall it increases compliance.[9-11] On the other hand, halothane impairs oxygenation and the elimination of carbon dioxide by the lungs, and, when combined with hypoxia, acidosis and mechanical airway stimulation, causes myocardial depression and increases myocardial irritability.[9] However, these problems can be overcome by administering a very high concentration of inhaled oxygen and 100 mmol/L of sodium bicarbonate just before intubation.

A Portex endotracheal tube (Portex Inc., Scarborough, Ont.) 8 mm or more in diameter should be inserted nasally to provide comfort and tube stability and to aid suction. If nasal polyps are present intubation should be done orally to prevent severe epistaxis.

Control of ventilation

A volume-cycled respirator must be used to ensure that the tidal volumes remain constant while the airway pressures are high and fluctuating. Respiratory rates of 8 to 12/min usually allow adequate time for expiration and inhibition of further air-trapping in an already overinflated lung. Low airflow rates reduce inspiratory pressures and ameliorate the adverse effect of the dependence of compliance on respiratory frequency, resulting in improved gas distribution and oxygenation. For adequate minute ventilation the tidal volumes should range from 10 to 12 mL/kg to allow the $Paco_2$ to fall at a controlled rate.

Systemic fluid balance is very important during IPPV. High peak inflation pressures, which often range from 40 to 80 cm H_2O, may cause profound hypotension through reduced venous return if the patient is dehydrated. Excessive hydration must also be avoided since the amount of water in the lungs can theoretically be increased to deleterious levels in these patients.[12]

The use of positive end-expiratory pressure is generally considered to be contraindicated in patients with asthma because the functional residual capacity and peak inspiratory pressures are already high. However, there is no uniform agreement on this point. Qvist and colleagues[13] believe that a positive end-expiratory pressure of up to 25 cm H_2O can combat air-trapping and thus recommend its use when conventional methods of management have not been successful.

If minute ventilation can easily be increased with IPPV, precipitous lowering of the $Paco_2$ must be guarded against, as it may lead to alkalosis, with arrhythmias, seizures and increased bronchospasm.[14] If, however, the high airway resistance limits effective minute ventilation, a low pH must be controlled with sodium bicarbonate until the bronchospasm begins to subside and the hypercapnia can be corrected.[15]

Maintenance of airway patency

For the maintenance of airway patency the patient's hands may initially have to be tied down to prevent self-extubation, a potentially fatal occurrence that complicates up to 13% of all intubations.[16] The frequent suctioning required can increase the bronchospasm, but this problem can be overcome with the instillation of 40 mg of lidocaine in 5 to 10 mL of normal saline 5 minutes before suctioning. In vitro, lidocaine prevents muscle tissue from responding to various stimuli;[17] specifically, it has been shown to prevent trachealis muscle contraction and mediator release in passively sensitized lungs of guinea pigs exposed to antigen.[18]

Bronchopulmonary lavage of secretions is extremely hazardous and has not been proven useful except in uncontrolled studies.[6,19] Unless there is evidence of atelectasis due to proximal airway obstruction the benefits of this procedure are probably outweighed by the risks. It should therefore be done in conjunction with bronchoscopy and only when conventional measures have failed.

Sedation and paralysis

Large doses of a sedative are often required during mechanical ventilation. Patients are frightened and often uncooperative, and they cannot coordinate their breathing with the respirator; these factors result in a dangerously high inspiratory pressure and an inadequate tidal volume. Morphine is frequently used,[20-22] but we feel its use should be reconsidered. The use of opiates, including morphine and meperidine, can provoke histamine release, bronchospasm, vomiting, aspiration and

Table II—Aspects of management of an asthmatic patient requiring mechanical ventilation

Maintenance of airway patency
Large endotracheal tube
Hand restraints
Frequent suctioning
Ventilation
High tidal volumes
Low respiratory rate
Low airflow rates
Acid–base and fluid balance
Monitoring of central venous pressure
Replacement of glucose and potassium
Administration of sodium bicarbonate for severe acidosis
Sedation
Intravenous administration of diazepam
Paralysis
Intravenous administration of pancuronium bromide
Maximal bronchodilation
Salbutamol inhalation
Continuous aminophylline infusion
Methylprednisolone administration
Isoproterenol infusion
Halothane inhalation
Infection control
Repeated cultures
Treatment of identified infection
Extracorporeal membrane oxygenation
Repeated reassurance and explanations

drying of respiratory secretions, facilitating inspissation, and in large doses may cause seizures.[9]

We favour the use of diazepam because it relieves anxiety, causes hypnosis and indirectly relaxes the muscles of the chest wall, thus increasing compliance. Repeated doses of 5 to 10 mg administered intravenously cause minimal depression of blood pressure, cardiac output and ventricular stroke work, and the therapeutic:toxic dose ratio is high.[9] Large doses are usually required to achieve the desired effect; Labrousse and coworkers[21] suggested an average dose of 185 ± 177 mg.

Diazepam in large doses is frequently all that is required to control ventilation,[22] but occasionally a neuromuscular blocking agent is required in addition.[23,24] This approach permits synchronization of the patient's breathing with the ventilator, increases chest wall compliance and decreases total body oxygen consumption. We strongly favour pancuronium bromide because succinylcholine chloride and tubocurarine chloride cause histamine release, and gallamine triethiodide increases the blood pressure and heart rate.[24] Pancuronium, a bis-quaternary ammonium steroid synthesized in 1964, is a competitive neuromuscular blocking agent with no histamine-releasing action and minimal cardiovascular effects and ganglionic blocking action.[24] The effect of a single dose of 0.04 to 0.10 mg/kg is reversed in 20 minutes, although repeated doses accumulate with tissue saturation.

Bronchodilation

Beta-agonists, theophyllines and corticosteroids are the safest and most effective bronchodilators. It is therefore important to ensure optimal use of these conventional drugs in patients with worsening asthma, especially before more hazardous and unproven treatments are used.

For highly selective β_2-agonists, such as salbutamol, inhalation is the preferred route of administration in terms of speed of onset, potency and lack of adverse systemic effects.[25,26] While isoproterenol and salbutamol in equivalent inhaled doses produce a similar degree of bronchodilation, the latter has a longer duration of action and is less likely to produce tremor and cardiovascular effects.[27] The intravenous route of administration is no more effective for salbutamol than the nebulized route, as judged by changes in the partial pressure of oxygen in arterial blood (Pa_{O_2}) and the FEV_1, yet the former route more often causes untoward effects, such as tremor, agitation, tachycardia and ectopic beats.[28] Although the generally recommended single dose of nebulized salbutamol varies from 1.25 to 5.0 mg, the safe maximum dose is probably much higher. For example, Light and associates[27] proposed 10 mg as the optimal single dose. Higher doses produce progressive bronchodilation but only at the expense of more side effects. No serious adverse effects have been noted with 10 mg,[27,28] but the actual amount of the drug that enters the respiratory tract is unknown and varies with the inhalational apparatus.

Isoproterenol produces 10 times the cardiac effect and 5 times the bronchodilator effect of salbutamol when given intravenously in equivalent doses.[20] Most experience with the use of isoproterenol in cases of severe asthma has been in children. Wood and collaborators[29] found that 27 of 35 children who would otherwise have undergone mechanical ventilation improved with intravenous doses of isoproterenol. However, Parry and colleagues[30] reported that 21% of the children in their study who had a Pa_{CO_2} above 40 mm Hg and were treated with isoproterenol, 0.1 to 0.6 $\mu g/kg \cdot min^{-1}$, still required mechanical ventilation. They compared these findings with those in a historical control group of asthmatic children with a similar Pa_{CO_2} who were not given isoproterenol: 19% of this group required mechanical ventilation. Whether the two groups matched in other characteristics affecting outcome is not known. Serious complications of treatment with isoproterenol are rare, and no drug-related deaths have been reported.[1,30,31]

Although intravenously administered isoproterenol is a potent bronchodilator, it has not been adequately studied in adults with asthma. Complications may include cardiac arrhythmias and a transient fall in the Pa_{O_2} from pulmonary vasodilation, which will result in ventilation–perfusion mismatch. Its use would therefore be justified only in an asthmatic patient who has undergone mechanical ventilation but continues to worsen despite treatment with selective β-agonists, aminophylline and corticosteroids.

Aminophylline's effectiveness is dose-dependent in the therapeutic range, and the drug has considerable toxicity above this range. Therefore, a serum theophylline level between 44 and 100 μmol/L (10 and 20 μg/mL) should be maintained at all times.[32] In a patient who has not previously taken aminophylline a total loading dose of 6 mg/kg should be administered at a rate no greater than 0.2 $mg/kg \cdot min^{-1}$ and be followed by a constant infusion of 0.5 $mg/kg \cdot h^{-1}$.[32] Frequent monitoring of the serum theophylline level is necessary since many factors may be present in asthmatic patients that alter the drug's disposition. For example, the use of erythromycin, cimetidine or oral contraceptives or the presence of a viral infection may reduce the rate of clearance. If the level is subtherapeutic it can quickly be corrected with an additional bolus that is half of the difference between the desired and actual serum concentrations as measured in micrograms per millilitre. If the level is too high the infusion should be discontinued in accord with the serum half-life, which, although highly variable, averages 5 to 6 hours.

Aminophylline has also been shown to increase the contractility and endurance of the diaphragm. This effect, which occurs in the therapeutic dose range, may prove to be of significant clinical benefit to the asthmatic patient with respiratory failure.[33]

The underuse of corticosteroids has been implicated in the deaths of asthmatic patients,[23] yet the toxic effects of these agents are negligible.[1] Short-course corticosteroid therapy is considered safe even in the presence of infection.[9] Methylprednisolone, which has approximately 125% the corticosteroid effect of prednisone when given in equal doses and less mineralocorticoid effect, with less resultant disturbance in the potassium and sodi-

um levels, is recommended in doses as high as 250 mg or greater, administered every 6 hours.[3] Although no clinical trials have determined the highest effective dose of methylprednisolone, underuse is the real danger. One useful indicator of inadequate dosage is failure of the eosinophil count to fall below 50×10^6/L within 36 hours.[34,35]

Ipratropium bromide is a poorly absorbed derivative of atropine. Administered as a metred aerosol (40 μg per puff) it produces significant bronchodilation within 20 minutes and a maximum effect within 60 to 120 minutes.[36,37] Its side effects appear to be minimal, unlike those of atropine, which include significant tachycardia, mydriasis and drying of respiratory secretions.[38] Whether ipratropium will prove to be a useful addition to the standard therapy we have outlined remains to be proven.

Halothane, with its bronchodilating effect, is another therapeutic tool for worsening asthma. Although not generally accepted management, the administration of 1% to 3% halothane has been used successfully in a few patients who have undergone mechanical ventilation and have not responded to more conservative therapy.[10,11]

Although there have been reports of treatment with other bronchodilating agents, such as rectally administered ether and inhaled atropine, maximum effective use of β-agonists, aminophylline and corticosteroids, in conjunction with proper ventilation, sedation and paralysis, is usually all that is necessary for the successful management of patients who are undergoing mechanical ventilation.

In summary, a reasonable approach for aggressive bronchodilation includes the immediate administration of methylprednisolone in large doses, of aminophylline in doses high in the therapeutic range and of nebulized salbutamol, 2.5 to 10.0 mg every 2 to 3 hours, as indicated by the therapeutic response and the appearance of adverse effects. Only if the patient's condition continues to deteriorate does intervention with controversial measures become necessary in an attempt to prevent the patient's death. The intravenous use of isoproterenol given in increasing doses, titrated according to the results of cardiac monitoring and the arterial blood gas levels seems justified. The use of halothane and selective bronchoscopic lavage would be final considerations.

Extracorporeal membrane oxygenation

If all forms of management fail to provide adequate gas exchange, or if serious barotrauma occurs, we suggest that the patient undergo extracorporeal membrane oxygenation (ECMO) until the disease process has been corrected. Asthmatic patients are ideal candidates for ECMO in that their disease process is reversible and they generally are young and have no underlying malignant disorder, bleeding diathesis or multisystem failure.

Conclusion

With optimal use of currently available therapeutic modalities the rate of death from asthma should continue to decline, even in patients with respiratory failure. However, in spite of changes in methods of critical care, it is likely that preventive care has the greatest potential to decrease the rates of illness and death in asthma since most patients can easily be treated by an interested and informed physician. Although in a few patients the asthma is highly labile and accompanied by rapid-onset respiratory failure, most admissions to hospital for status asthmaticus are thought to be preventable.[3,22] Once the life-threatening situation has passed, the most important aspects of management — education, medication and close follow-up — must begin.

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