Invasive and Noninvasive Ventilation in Patients With Asthma

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Despite recent advances in our ability to manage asthma, there continues to be a small but important incidence of patients who present with severe asthma exacerbations that require ventilatory support. Mechanical ventilation in these patients is difficult and can be associated with substantial morbidity. Unfortunately, there is little in the way of randomized controlled trials to guide our therapeutic decisions in these patients. The goal is to provide adequate gas exchange while minimizing hyperinflation and ventilator-induced lung injury and administering aggressive therapy to reduce airway inflammation and bronchoconstriction. Although there is controversy on exactly what is the optimal method for mechanical ventilation in asthma, most experts agree that a general approach based on controlled hypoventilation is ideal. *Key words: asthma, hypoventilation, exacerbation, mechanical ventilation.* [Respir Care 2008;53(6):740–748. © 2008 Daedalus Enterprises]

Introduction

One of the most challenging aspects of respiratory care is the management of the patient with status asthmaticus who requires ventilatory support. Although the incidence and prevalence of acute severe asthma episodes that require ventilatory support are relatively unknown, the asthma

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The author reports no conflicts of interest related to the content of this paper.

Dr Medoff presented a version of this paper at the 41st RESPIRATORY CARE Journal Conference, "Meeting the Challenges of Asthma," held September 28-30, 2007, in Scottsdale, Arizona.

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hospitalization and death rates have declined in recent years, which suggests a concurrent decline in the need for mechanical ventilation of patients with asthma.[1,2] That decline, despite an increased prevalence of asthma, probably reflects our improved ability to manage asthma on a long-term basis and early during exacerbations. However, patients continue to present with severe exacerbations that require mechanical ventilation, and mortality may approach 10% in these patients.[2] Thus, we must remain familiar with the care of these critically ill patients and maintain an in-depth understanding of respiratory failure in asthma.

There are very few comprehensive data regarding the rate of severe asthma episodes and the incidence of asthma respiratory failure that requires mechanical ventilation. According to the most recent United States Surveillance for Asthma, for the 3-year period 2001-2003, an average annual 20 million persons in the United States had asthma.[1] Among those persons, asthma caused an average annual 1.8 million emergency-department visits, 504,000 hospital discharges, and 4,210 deaths. Thus, using the number of emergency room visits and hospitalizations as a surrogate for asthma exacerbations, around 5–10% of asthmatics experience a major exacerbation in a given year. Of those patients, a small but important percentage require mechanical ventilation.

Recent reports of asthma-related intensive-care-unit morbidity and mortality reported an intubation rate of 2–20 patients per year and a death rate of 1–26.7% of intubated patients.[2] Thus, asthma-induced respiratory failure that requires mechanical ventilation remains a noteworthy problem in the care of asthma. Unfortunately, we have little in the way of randomized trials to guide the care of these patients, and they can be extremely difficult to manage. My approach to the management of these patients is based on an understanding of the complex physiology of severe asthma and clinical experience. In this review I will present a practical management plan based on the pathophysiology of respiratory failure in asthma and the existing literature. This review will focus on the care of adult patients, although some of the issues discussed will also be applicable to pediatric patients. The management of pediatric patients with asthma that requires mechanical ventilation has been reviewed elsewhere.[3,4]

Pathophysiology of Life-Threatening Asthma

Life-threatening asthma results from severe exacerbation that puts the patient at risk of asphyxiation. It follows that the more severe the exacerbation, the higher the risk of mortality. Unfortunately, it can be difficult to classify the severity of an exacerbation. According to consensus guidelines, an asthma exacerbation is considered severe when the patient meets specific criteria (Table 1).[2,5-7] In addition, patients with certain historical patterns of asthma are more likely to have a severe exacerbation (Table 2). However, it is important to note that over 50% of patients who have a life-threatening asthma episode may not have suggestive histories or disease patterns. Thus, any patient with asthma can present with a life-threatening exacerbation at any time.

Table 1. Definition of a Severe Asthma Exacerbation*

Accessory muscle activity
Paradoxical pulse > 25 mm Hg
Heart rate > 110 beats/min
Respiratory rate > 25–30 breaths/min
Limited ability to speak
PEF or FEV_1 < 50% of predicted
Arterial oxygen saturation < 91–92%

* One or more of these criteria constitute a severe exacerbation.
PEF = peak expiratory flow
FEV_1 = forced expiratory volume in the first second

Table 2. Risk Factors for Severe Asthma Exacerbation*

Prior mechanical ventilation
Prior intensive care unit admission
Recent hospitalization
American Thoracic Society definition of severe asthma[7]
Poor adherence to therapy
High allergen exposure

* < 50% have risk factors.

The major physiologic changes associated with a severe exacerbation are airflow limitation, bronchial hyperresponsiveness, airway closure, loss of elastic recoil, and hyperinflation (or air trapping). These all result from airway narrowing, largely due to bronchoconstriction, although edema and mucus production in the airways also probably contribute to the reduction in airway caliber. In fact, autopsy studies of patients who died of asthma indicate a high incidence of airway obstruction from mucus impaction,[8,9] which suggests that edema and mucus production may play a more prominent role in severe exacerbations.

It is important to note that research shows that the basis of the edema, mucus production, and bronchoconstriction in asthma is airway inflammation. In general, the airway inflammation characteristic of asthma results from an immune reaction to an inhaled antigen or infectious agent from the environment. In allergic asthma, the airways develop predominantly eosinophilic inflammation. In nonallergic asthma, neutrophilic and pauci-immune forms have been described, but it is unclear if these represent distinct clinical phenotypes, as they often respond to conventional asthma therapy.[10] Some data suggest that neutrophilic forms are more often associated with severe or refractory asthma

and thus may be more common in those presenting with severe exacerbations.[11,12] In response to the airway inflammation, airway smooth-muscle cells become hyperreactive, leading to reversible bronchoconstriction in response to various stimuli. Based on this understanding of asthma pathogenesis, the current approach to therapy for asthma exacerbation includes bronchodilators to relieve bronchoconstriction and anti-inflammatory therapy (ie, corticosteroids), which is critical for the ultimate resolution of an exacerbation.

The airway narrowing increases the resistance to airflow and requires the patient to work harder to breathe. The increased resistance lengthens the exhalation time required to empty the lung, which leads to air trapping (hyperinflation). In addition, factors such as low pulmonary elastance and persistent activation of the inspiratory muscles contribute to the tendency for air trapping.[13-17] Hyperinflation stimulates the feeling of dyspnea, impairs gas exchange by increasing dead space, increases the work of breathing, and in extreme cases leads to hemodynamic compromise and barotrauma. Unfortunately, mechanical ventilation, when improperly managed, can exacerbate hyperinflation by increasing the minute ventilation. Thus, it is not surprising that mechanical ventilation of a patient with asthma can be associated with increased dead-space ventilation, barotrauma, and hemodynamic collapse (caused by effects on venous return).

Recent research suggests that the pattern of airway narrowing is heterogeneous, leading to lung areas with relatively preserved ventilation near areas with high-grade obstruction (Fig. 1).[18,19] Indeed, some airways may be completely obstructed by severe constriction and mucus impaction and thus may trap gas in the lung at high pressure.[17,20] The implication is that routine measurements of end-inspiratory and end-expiratory pressure, used to judge the safety of ventilation, may underestimate the amount of trapped gas in the patient, as has been described clinically.[20] Thus, this heterogeneity contributes to the complexity of ventilation and makes it more likely to have unrecognized hyperinflated regions that lead to poor ventilation-perfusion matching, hemodynamic compromise, and increased susceptibility to barotrauma.

The consequences of these physiologic changes on ventilation are profound. Changes in the delivered pressure or volume, inspiratory time/flow, respiratory rate, and positive end-expiratory pressure (PEEP) can all influence the degree of air trapping.[21,22] Furthermore, hyperinflation can go unrecognized, and there are no perfectly reliable tests for "safe" ventilation. Given this complexity, a careful and "personalized' approach to ventilation of these patients is warranted, based on our understanding of the physiology of severe asthma.

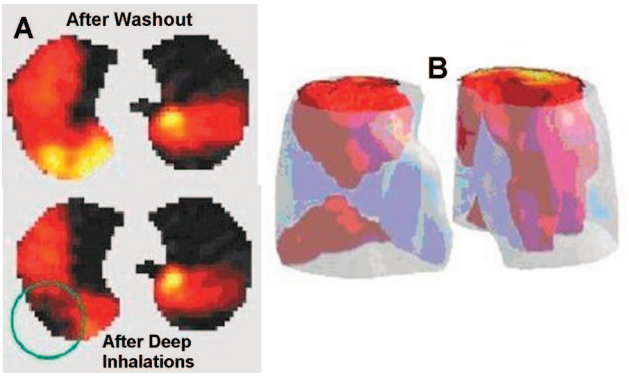

Fig. 1. A: Positron emission tomogram of residual intrapulmonary tracer gas in a lung cross-section from a patient with asthma. The tracer concentration increases according to the following color scale: black (no tracer), red, yellow, white (most tracer). The insoluble tracer is washed out during breathing or is retained inside large ventilation defects. After deep inhalations (lower panel), tracer clearance is enhanced from parts of these defects (circle). B: Volumetric rendering of ventilation defects (red) and the external surface of the lungs (blue). The image orientation is as if the subject were standing facing the reader. These images demonstrate the heterogeneity of ventilation in asthmatic lungs. (From Reference 19, with permission.)

Goals of Mechanical Ventilation in Asthma

In this review I will not cover the indications for intubation. as this is reviewed in another manuscript from this conference.[23] Once the patient is intubated, the primary focus of mechanical ventilation should be achieving adequate oxygenation (oxygen saturation 88–92%) and ventilation, while minimizing hyperinflation. To achieve those goals it is often necessary to hypoventilate the patient. Important considerations are determining exactly what is a "safe" amount of hyperinflation and what are the minimal ventilatory requirements (ie, arterial blood pH $>$ 7.20). Unfortunately, there have been few randomized controlled trials to guide us. Case series have suggested that hypoventilation and moderate respiratory acidosis can be well-tolerated in these patients,[24,25] although the exact cut-off of a "safe" pH has not been determined. In addition, Tuxen et al found that the incidence of complications can be reduced by limiting hyperinflation below a critical value (assessed by measuring the exhaled tidal volume [V_T] after a 40–60 s prolonged expiratory pause maneuver).[26] Others have recommended pressure or volume limits (plateau pressure $<$ 30 cm H_2O, V_T 8–10 mL/kg) based on normal physiology, but the safety of that type of approach has not been validated.[27]

It thus appears prudent to take an approach of "controlled hypoventilation" or "permissive hypercapnia," with a minute ventilation that maximizes expiratory time (thus minimizing hyperinflation), but provides enough ventilation to keep the arterial CO_2 and pH in a reasonable range.[17]

Table 3. Initial Ventilator Settings

Pressure or volume ventilation per individual or institutional preference and patient characteristics
Avoid air-trapping
T_I 0.8–1.2 s (high flow, constant rather than descending-ramp flow)
f 10–15 breaths/min
V_T 6–8 mL/kg
$P_{plat} < 30$ cm H_2O
PEEP 0 cm H_2O
F_{IO_2} adequate to provide S_{pO_2} 88–92%

T_I = inspiratory time
f = frequency (respiratory rate)
V_T = tidal volume
P_{plat} = plateau pressure
PEEP = positive end-expiratory pressure
F_{IO_2} = fraction of inspired oxygen
S_{pO_2} = blood oxygen saturation measured via pulse oximetry

The safe range of these values depends in part on certain characteristics of the patient's condition (eg, hemodynamic stability, arrhythmias) and the clinical judgment of the care team.

Setting the Ventilator

Table 3 shows a recommended set of initial ventilator settings for the intubated asthmatic patient.

Mode

The first decision to be made is the ventilation mode. This choice may be influenced by institutional preference, but there are clear advantages and disadvantages to both pressure-targeted and volume-targeted strategies. In a pressure-targeted mode the peak inspiratory pressure is limited and the lungs will not be inflated to a pressure above the set peak pressure. This has the advantage of always limiting the amount of hyperinflation. For example, if pressure control is used with an inspiratory pressure of 30 cm H_2O, the pressure in the lung will not exceed 30 cm H_2O, even if there are occluded airways with trapped gas. Another advantage of a pressure-targeted mode is that if the airway resistance suddenly increases, the patient will not hyperinflate; however, the V_T will drop. The problem with a pressure-targeted mode is that if the airway resistance is very high, it will be difficult to deliver an effective V_T.

In my experience I have found it very difficult to provide adequate ventilation (arterial pH > 7.20) to severely obstructed patients with pressure control. This is largely due to the mechanics of delivering a V_T against a high resistance with a low pressure limit. The smaller V_T also makes it more difficult to deliver aerosolized bronchodilator. Thus, a pressure-targeted mode will provide the safest form of ventilation, but at the expense of decreased CO_2 clearance, a lower pH, and less effective aerosol delivery. It should also be noted that as the patient's airflow obstruction improves, a high pressure setting with a pressure-targeted mode could lead to a large V_T. Thus, as the patient improves, the pressure setting should be reduced accordingly.

A volume-targeted approach will better provide a minimal V_T by delivering very high flow and pressure that overcome the high airway resistance. This provides better ventilation and aerosol delivery but increases the risk of hyperinflation. Often we monitor plateau pressure after a volume-targeted breath as a surrogate for end-inspiratory lung volume (which should best track with the risk of barotrauma). However, the plateau pressure is an average pressure and will reflect only the pressure in open lung units. Lung areas that have high pressure in the initial part of the inspiratory cycle, and lung segments that become occluded at the end of inspiration, may still be at risk of barotrauma despite a "safe" plateau pressure. Thus, a volume-targeted ventilation mode will better ensure adequate ventilation in severe cases or with abrupt increases in airways resistance, but probably increases the risk of hyperinflation in the asthmatic patient. My strategy is to use pressure control when possible, but in most cases I need to start with a volume-targeted approach and carefully monitor for signs of hyperinflation.

Minute Ventilation, Tidal Volume, and Respiratory Rate

The risk of hyperinflation will track directly with the minute ventilation. Most experts recommend limiting V_T in ventilated asthmatic patients to 6–10 mL/kg. I usually use small V_T (6–8 mL/kg), based in part on the experience in patients with acute lung injury.[28] Although asthmatic patients may not have the same risk of ventilator-induced lung injury as do patients with acute lung injury, some data suggest that reducing V_T in all patients with respiratory failure may reduce the risk of ventilator-induced lung injury.[29]

Inspiratory Time and Inspiratory Flow

In the end, the most critical determinant of hyperinflation in a mechanically ventilated asthmatic patient is the expiration time. The longer a patient exhales, the less gas will be trapped in the lung at end-expiration, which reduces the risk of hyperinflation during inspiration. One can maximize expiratory time for a given minute ventilation by shortening the inspiratory time. In volume-targeted modes this is accomplished by increasing the inspiratory flow rate and using a constant-flow pattern (as opposed to

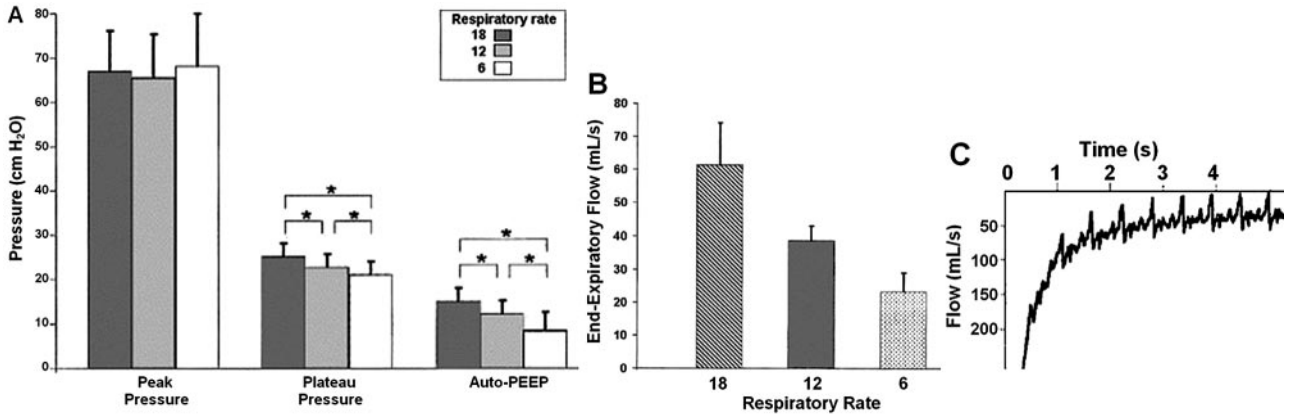

Fig. 2. A: Peak airway pressure, plateau pressure, and intrinsic positive end-expiratory pressure (auto-PEEP) at respiratory rates of 18, 12, and 6 breaths/min, in 12 patients with asthma. B: End-expiratory flow at respiratory rates of 18, 12, and 6 breaths/min, in 7 patients. C: Representative expiratory flow tracing from an individual patient, demonstrating plateau of the flow rate. (From Reference 30, with permission.)

a variable pattern). In pressure-targeted modes the flow rate is determined in part by the patient's inspiratory drive, so there is much less ability to control the flow rate in a pressure-targeted mode. It is important to note that recent research suggests that there is a plateau in expiratory flow after a certain point, so increasing the expiratory time above a certain value has limited benefit. In general, after about 4 seconds of expiration there is nominal gain in reducing hyperinflation (Fig. 2).[30] One must also consider the consequences of a high constant-flow rate. Higher airway pressure and a more heterogeneous distribution of ventilation will result when inspiratory flow is high, which can increase the risk of focal areas of hyperinflation and make ventilation less effective by increasing dead space. Based on this, I favor a moderately high flow rate (60–80 L/min) with a descending flow pattern, targeting an inspiratory time of 0.8–1.2 seconds.

Fraction of Inspired Oxygen

Oxygen-enriched gas should be administered to all ventilated asthmatic patients, but the fraction of inspired oxygen needs to be only enough to provide a blood oxygen saturation greater than 88%. It is important to note that bronchodilators can decrease oxygen saturation by dilating the pulmonary vasculature and reducing ventilation-perfusion matching.

Positive End-Expiratory Pressure

The application of PEEP in status asthmaticus is controversial. In patients with emphysema, PEEP can counterbalance the intrinsic PEEP (auto-PEEP) without affecting expiratory flow because of dynamic collapse of the airways and a "waterfall effect."[31] This can be helpful in patients who are spontaneously breathing, because it improves ventilator triggering. However, in asthmatics the site of increased resistance is in central (less collapsible) airways.[32] Furthermore, asthmatic airways are likely to be stiff (from inflammation) and more resistant to dynamic collapse, and thus will not have the same waterfall effect as in patients with emphysema.[31,33] If there is no dynamic collapse, then, in theory, the use of PEEP will increase the back-pressure to expiratory flow and result in more hyperinflation. Indeed, early physiology studies of asthmatics on ventilators demonstrated that the application of PEEP led to more hyperinflation.[33,34] Thus, most review articles have not recommended the routine use of PEEP in asthmatic patients.[17,27] However, a recent study suggested that the physiology may be more variable, so some patients respond to PEEP with increased air trapping, some with no change in lung volume, and some with a paradoxical decrease in lung volume (Fig. 3).[35] This would suggest that in some patients PEEP can be carefully applied, although my current practice is to use no PEEP during controlled ventilation.

Monitoring for Hyperinflation

Once the patient is intubated and stabilized on the initial ventilator settings, the care team must frequently monitor for hyperinflation, using one or more maneuvers. Assuming the patient is not spontaneously breathing and is in synchrony with the ventilator, the end-inspiratory (plateau) and end-expiratory (auto-PEEP) pressures should be measured shortly after every change in ventilator settings, and periodically when on stable settings. The plateau pressure is a surrogate for the lung volume at end-inspiration, which directly correlates with the risk of barotrauma. Auto-PEEP can be used as a measure of the degree of airway obstruction and to assess the risk of hemodynamic compromise related to hyperinflation. In general, we target auto-PEEP less than 5 cm H_2O and plateau pressure less

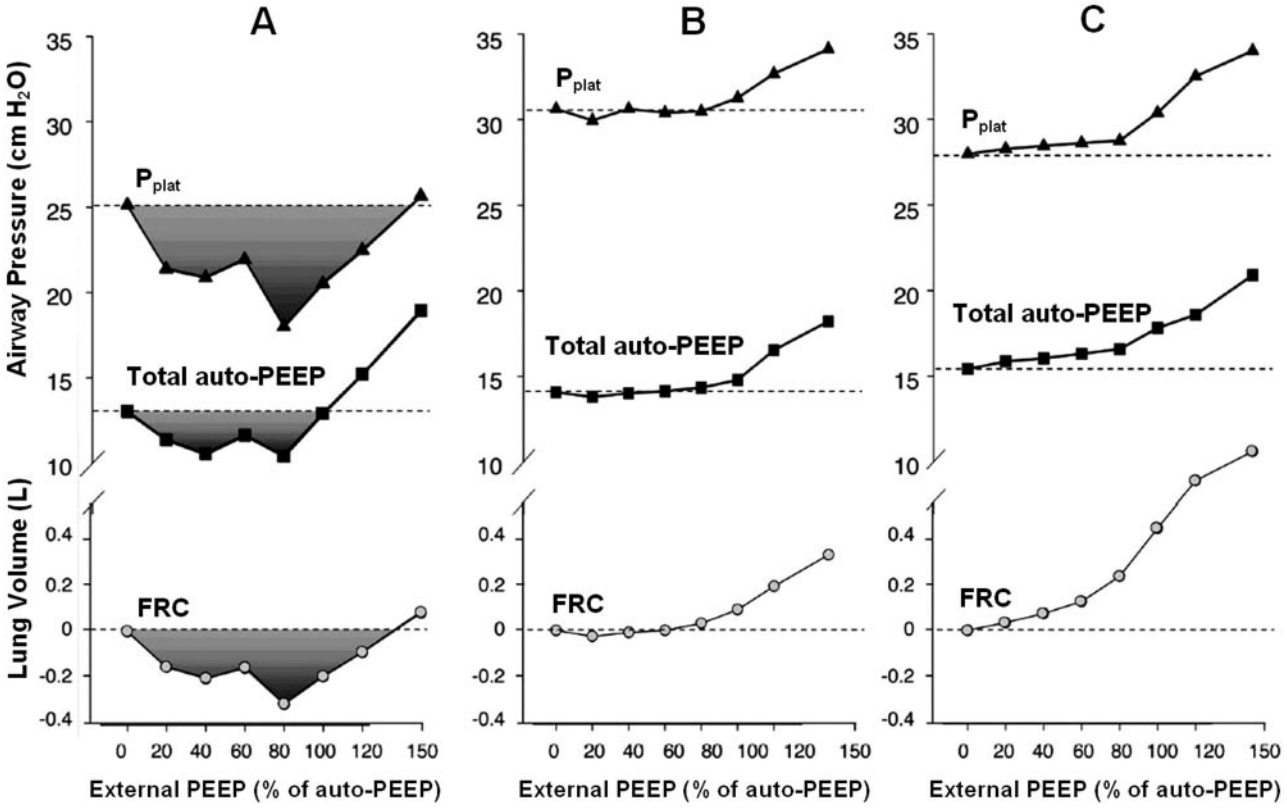

Fig. 3. Three of the possible responses observed in plateau pressure (P_{plat}), total intrinsic positive end-expiratory pressure (auto-PEEP), and functional residual capacity (FRC) with the application of PEEP (represented as a percentage of auto-PEEP). The FRC measured at zero external PEEP was considered the reference. Changes were independent of ventilator settings. A: Paradoxical response with a decrease in lung volumes. B: Biphasic response: initially there is no change in lung volume, until the applied PEEP reaches about 80% of the auto-PEEP. C: Overinflation response: there is increased air trapping as PEEP increases. (From Reference 35, with permission.)

than 30 cm H_2O, but it is important to realize that these measurements represent average pressures, so some lung areas might be exposed to higher pressure than those measured with plateau pressure and auto-PEEP. In addition, as mentioned earlier, the standard auto-PEEP measurement does not reflect the pressure in lung areas behind obstructed airways at end-expiration.[20] This so-called occult-occult PEEP should be suspected in patients who have low measured auto-PEEP but high plateau pressure and evidence of hyperinflation on chest radiograph. Thus, one cannot assume that a patient is being safely ventilated, even if the auto-PEEP value is less than 5 cm H_2O and the plateau pressure is less than 30 cm H_2O.

The most predictive measurement may be the lung volume at end-inspiration.[26] For this measurement the patient is paralyzed and allowed to exhale for 40–60 seconds, following a period of stable ventilator settings. Data suggest that if the exhaled volume is less than 20 mL/kg, the patient's risk of barotrauma is low and no further changes to the ventilator settings are needed. However, the frequent use of this maneuver for routine monitoring is not practical, because paralytic therapy is relatively contraindicated in asthmatics because of the high risk of neuromuscular complications.[36-38] Thus, I continue to use the surrogate measurements of auto-PEEP and plateau pressure to guide ventilator settings in most asthmatic patients. In very severe cases in which the risk of barotrauma is high (or if barotrauma is already present), I will occasionally use the lung volume at end-inspiration to guide therapy. The real key is frequent assessments of the patient as the disease process evolves, because the degree of bronchoconstriction can change quickly, which often necessitates ventilator-setting changes.

Ancillary Therapy

It is crucial to realize that mechanical ventilation is able only to stabilize the asthmatic patient and does not treat the underlying inflammation or bronchoconstriction. Ancillary therapies such as corticosteroids and inhaled bronchodilators are critical components of the management of these patients. It is beyond the scope of this review to discuss the data on these agents, but I would like to comment on a few therapies that should be considered, especially in the most severe cases.

Sedation and Paralysis

All asthmatic patients on mechanical ventilation require some sedation for comfort and ventilator synchrony. Patients who require controlled hypoventilation will often require very deep sedation, and in some cases chemical paralysis will be necessary for management of the ventilator. One of the problems with mechanical ventilation in these patients is that they have a very high respiratory drive that results in an elevated respiratory rate. When the ventilator provides assistance, it allows the patient to take in a larger V_T, which can increase hyperinflation, dead space, and CO_2, and thus decrease pH, leading to an even higher drive to breathe. The only way to interrupt this cycle is to heavily sedate the patient and reduce the respiratory drive. Often, short-term paralysis (20–60 min) with neuromuscular blockade is needed to allow complete synchrony with the ventilator. Once the ventilator is completely in control of respiration, the patient can be ventilated with smaller V_T and a lower respiratory rate, which decreases hyperinflation, improves ventilation, and lowers respiratory drive. Shortly after the patient is stabilized with a lower CO_2 and higher pH, the paralytic can often be discontinued and the sedation reduced without a recurrence of the rapid respiratory rate and hyperinflation.

The benzodiazepine class of sedatives can be used with minimal adverse effects but are usually not sufficient to suppress respiratory drive. Opiates are potent suppressors of respiratory drive, but morphine can cause histamine release that can lead to hypotension and bronchoconstriction. Therefore, if an opiate is used, I recommend a synthetic form such as fentanyl. Propofol has many favorable properties, including rapid onset and offset, bronchodilation, and potent suppression of respiration. Unfortunately, it can cause profound hypotension and must be used with care.[39,40] Ketamine also is a good bronchodilator, but can increase respiratory secretions. Overall, I prefer propofol for sedation of asthmatics because of its potency and bronchodilating properties. However, propofol will cause hypotension, which should be managed with fluid boluses and may necessitate the use of vasopressors.

Neuromuscular blockade increases the risk of prolonged paralysis and myositis in asthmatic patients, but most of this risk is related to prolonged use of paralytics ($>$ 24 h). Short-term bolus neuromuscular blocker is probably reasonably safe.[36,37,41] I prefer cisatracurium, because it is largely metabolized by a process independent of liver and kidney function.

Intravenous Epinephrine

In severely obstructed patients it may be very difficult to deliver adequate doses of bronchodilator with the ventilator, especially if the ventilator cannot safely deliver a V_T larger than 300 mL (due to severe obstruction). In such cases, intravenous bronchodilators can be considered. If the patient is young and at low risk of coronary artery disease, I prefer to use a low-dose infusion of epinephrine, as opposed to intravenous β agonist. Epinephrine has the added advantage of α-receptor blockade, which leads to vasoconstriction and may help with hypotension, and, theoretically, may help reduce airway edema. There are no data that indicate improved outcomes with epinephrine infusions in asthma, but one study found that it can be used relatively safely, although there was an increased risk of myocardial ischemia.[42]

Other Therapies

In very severe cases there are other "salvage" therapies that can be considered but are supported by only anecdotal evidence. These include buffer therapy with bicarbonate or amino alcohol tromethamine (tris buffer or tris-hydroxymethyl aminomethane), inhaled anesthesia, airway clearance with bronchoscopy and mucolytics, helium-oxygen mixture (heliox), and extracorporeal membrane oxygenation.[17,27] Discussion of these therapies is beyond the scope of this review.

Noninvasive Ventilation

Given the complexity of mechanical ventilation in these patients, the best approach may be to try to avoid intubation. Noninvasive ventilation (NIV) often prevents intubation in patients with chronic obstructive pulmonary disease,[43] and therefore may have a similar benefit in patients with asthma. Unfortunately there have been only 2 small prospective trials of NIV in adults with status asthmaticus (47 patients total), so the published experience is limited.[44,45] However, both of these studies showed improvements in obstruction. The study by Meduri et al found improved gas exchange in a group of patients with baseline hypercapnia.[44] The study by Soroksky et al randomized patients to NIV or conventional therapy and found more rapid improvement in lung function and a significant reduction in the need for hospitalization. More recently, a Cochrane meta-analysis concluded that NIV in adult patients suffering from status asthmaticus remains controversial, despite some very promising preliminary results.[46] Although far from conclusive, these data suggest that NIV may be attempted in carefully selected asthmatic patients.

The first step in using NIV in asthma is selecting the appropriate patient. Ideally, the patient is compromised but not so impaired that respiratory failure is imminent. In general, I choose patients with mild to moderate respiratory distress, indicated by a respiratory rate greater than 25 breaths/min, the use of accessory muscles to breathe, or difficulty speaking. If blood gas analysis is available, I select patients with an arterial pH of 7.25–7.35 and a P_{aCO_2} of 45–55 mm Hg. I exclude patients with impending respiratory failure, who are not able to protect the airway (or have high aspiration risk),

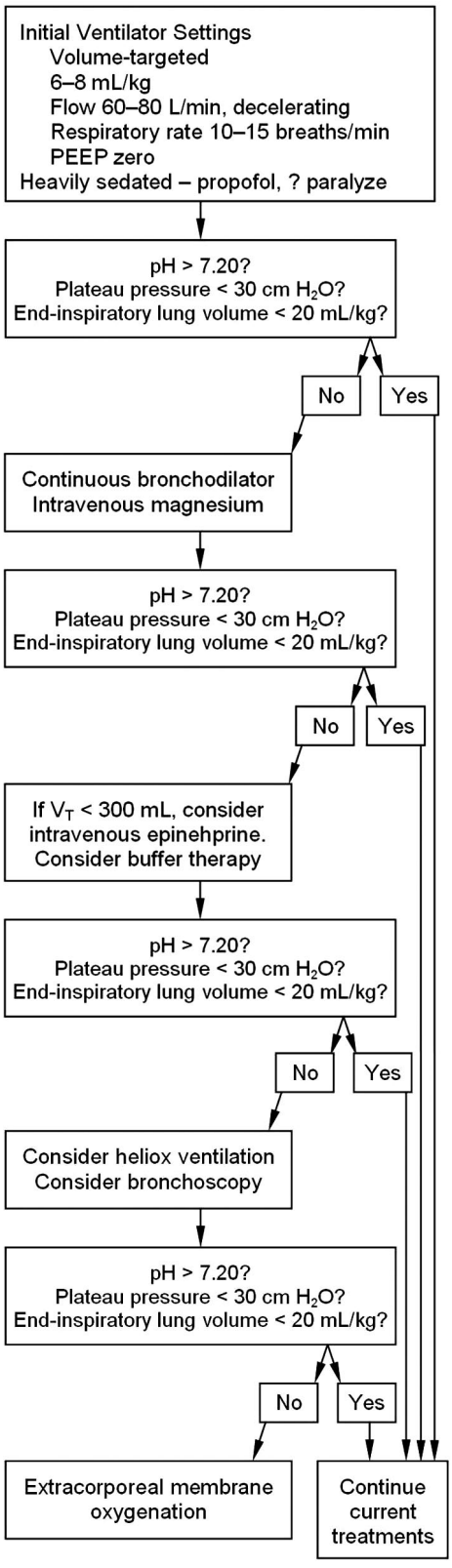

Fig. 4. Flow diagram of my general approach to ventilation of patients with asthma.

have unstable hemodynamics, have copious secretions, are unable to tolerate or fit the face mask (ie, recent facial surgery, craniofacial trauma or burns, anatomic lesion of the upper airway), or are uncooperative.

I usually start the patient on pressure-support ventilation, with a full-function ventilator. The face mask is carefully chosen so it fits properly, and the procedure is explained to the patient. The respiratory therapist then initiates NIV while holding the mask in place. Once it is clear the patient can tolerate the positive pressure, the mask is secured, but a tight fit is avoided. The inspiratory pressure is then titrated to patient comfort, and the expiratory pressure (PEEP) to a pressure that allows efficient triggering. The fraction of inspired oxygen is titrated to keep the blood oxygen saturation above 90%, and peak inspiratory pressure is limited to less than 20 cm H_2O. The therapist should continue to coach and reassure the patient and adjust the ventilator settings to assist the patient in tolerating and continuing the NIV.

In general, NIV is well tolerated, but one must observe for the following mild complications: air leaks, mask discomfort and facial soreness, eye irritation, sinus congestion, and oronasal drying. In addition, the patient must be continually assessed for ventilator asynchrony, gastric insufflation/aspiration, and hemodynamic compromise. Aspiration due to vomiting from gastric insufflation is a particularly dangerous complication and more likely with higher inspiratory pressure. If the patient is unable to tolerate or worsens on NIV, intubation should be considered immediately.

Summary

Mechanical ventilation of the asthmatic patient is complicated and requires careful personalized management. Based on the available data, it appears that a general approach based on controlled hypoventilation is ideal. The overall goals of ventilation should be to provide adequate gas exchange while minimizing hyperinflation and administering aggressive therapy to reduce airway inflammation and bronchoconstriction. Figure 4 summarizes my approach.

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Discussion

MacIntyre: I'm surprised that you are so down on pressure-control ventilation. I find it very easy to use. I like that you can limit the maximum pressure with it, and you give just enough pressure to deliver a tidal volume of 6 mL/mg. It's OK if that produces respiratory acidosis. I'm willing to live with a pH of 7.00 to 7.10, provided there's an adequate P_{O_2}. Respiratory acidosis does not kill you, so I'm very comfortable with that.

Medoff: Maybe that acceptance of acidosis is a product of age, because as I've gotten older, I've tolerated lower and lower pH, and I think it's partly experience. The interns call you at 7.3, the juniors at 7.25, the seniors at 7.2, and the fellows at 7.1. So part of it has to be your comfort with it, and with pressure-control ventilation I think I would prefer to do it, but it's what you're willing to tolerate.

MacIntyre: One of the paradoxical things you can get into is that if you give excessive tidal volume and excessive ventilation, you can produce more air trapping, more dead space, and the P_{CO_2} will rise. Then you get panicky and think, "Oh my goodness, he needs more ventilation," and you increase the tidal volume, create more dead space, and the P_{CO_2} gets even higher. So you can get caught in a circle that ends up with horrible overdistention injury.

Medoff: Sometimes the first thing to do is to reduce tidal volume and reduce your—what in the old days we called the west lung zone 1 or 2, where you've created that dead space by overventilating and hyperinflating.

Pierson:* I'd argue that the risk of overdistention may actually be greater with pressure control than with volume control in certain cases. In the setting of ARDS [acute respiratory distress syndrome] that argument rests on the heterogeneity of injury within the lung, and the most compliant areas are more distended. I believe the data support limiting both plateau pressure and delivered tidal volume in ARDS. In status asthmaticus you have the additional problem of more rapid physiologic improvement if things go well, than you see in most ARDS cases.

So if you have the patient set up on pressure control and keep the plateau pressure constant, as the patient's resistance and compliance improve, you will get more and more distention from that same pressure. So it would seem that with pressure control you would have to watch very closely that the distending tidal volume doesn't get out of control and increase more than you intended.

MacIntyre: Dave, you're right, but I'm not sure it's fundamentally different from volume control. With volume control you're putting in a set volume, and if resistance worsens, pressure can rise dramatically. You therefore have to monitor the pressure like crazy. And if the patient gets worse, you may have to promptly turn the tidal volume down. In pressure control you've just got to monitor the tidal volume, and if it starts getting bigger, you have to ratchet down the pressure. So I'm not sure if it's any more or less dangerous. It's just that with volume control you monitor pressure and adjust volume, and with pressure control you monitor volume and adjust pressure.

Pierson: I take your point, and I think the lesson here is the need for very close monitoring of both pressure and tidal volume in whichever of those modes you choose.

MacIntyre: You mentioned an article in which adding PEEP [positive end-expiratory pressure] decreased the functional residual capacity. I found that article interesting as well.[1] My explanation—and I've seen this on a couple of occasions—is that there's a triggering problem, and the patient's very dyspneic because of the triggering problem. When you give them a little PEEP, they can trigger more easily and their respiratory drive then decreases, so their minute ventilation, intrinsic PEEP, and functional residual capacity all fall, because there's less air trapping.

1. Caramez MP, Borges JB, Tucci MR, Okamoto VN, Carvalho CR, Kacmarek RM, et al. Paradoxical responses to positive end-expiratory pressure in patients with airway obstruction during controlled ventilation. Crit Care Med 2005;33(7):1519-1528.

Colice: Asthma is not like ARDS. In ARDS the problem is in the alveoli, whereas in asthma the problem is in the airways. If you have an airways disease—which in severe asthma is almost all the airways—it's not heterogeneous any more, almost all the airways are involved—the plateau pressure is not really telling you the alveoli pressure. It tells you the pressure in the airways, because you're not effectively ventilating most of the alveoli. So what I would worry about is not the plateau pressure but the PIP [peak inspiratory pressure], which is the pressure that's driving air into the alveoli. That's really what causes overdistention. So why are you focusing on the plateau pressure and not the PIP?

Medoff: That's an excellent point. All the airways are affected, and the heterogeneity is in the degree of severity. The plateau pressure measures only the pressure in airways and alveoli that are in communication. There's no flow at that point, so the pressure is what it is, and it's the average of the open units in the lung at that point. Transpulmonary pressure is 30 cm H_2O for total lung capacity, so you're not overdistending units at that pressure. Based on some observational

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studies, risk of barotrauma is lower at this pressure. But you're right that if the PIP is higher than the plateau pressure, there are some units exposed to pressures higher than plateau pressure.

The problem is that much of the PIP is a function of tube resistance and airways resistance, which isn't necessarily damaging to the lung. So I think we're able to tolerate that. And when people have looked at what tracks with barotrauma, it's not the PIP, it's the plateau pressure, which is probably a better measure of overdistention.

But the caveat is that you still see an incidence of 1–3% pneumothoraces with "safe" ventilation practices. So, clearly, some units are getting more with that. I would echo what Neil said earlier: you have to be aware of the PIP, and I think an effort to limit PIP—again arguing that maybe pressure control is better because it won't get higher than the set pressure, although you have to monitor these things carefully.

Colice: Your assumption is the plateau pressure reflects alveoli pressure, and that assumption is not proven, I think, because the plateau pressure tells you the pressure in the circuit during a steady-state condition and that pressure is a combination of pressures in the airways.

Medoff: It's every open lung unit. Assuming your flow goes to zero, the pressure has to be the same throughout, so if an alveolus and an airway are open and there's no flow, the pressure has to be the same across there. If there's a pressure difference, there'll be flow.

Colice: Right, but you also have to assume that the airways are obstructed.

Medoff: So if I have a unit that is overdistended but closed, I won't detect it with a plateau pressure measurement.

Colice: But that plateau pressure will reflect the pressure proximal to the airway obstruction.

Medoff: Correct. The plateau pressure only reflects the open lung units, so I'm saying go as low as you can go when you ventilate these people. I think the idea of a safe plateau pressure is erroneous, and the problem is that to get volumes in some patients requires higher pressure on the PIP side. Does that answer the question?

Colice: Well, it's an answer. I'm still not sure.

Medoff: I expected more trouble about the intravenous epinephrine.

Myers: You alluded to your bias for pressure-control ventilation. What about dual-control ventilation that's supposed to give you the benefits of pressure control but guarantees a set volume?

Medoff: At Massachusetts General we have not really used these new pressure-limited volume-control modes. Theoretically, they sound great as a way to get the best of both worlds. I still think the name of the game with this is sitting at the bedside and watching the patient's condition evolve, and limiting the tidal volume and ventilation, and hopefully the patient will turn around. The amazing thing is how quickly they can turn around when they do.

MacIntyre: I'm not sure pressure-regulated volume-control ventilation is the best of both worlds. It's a compromise, because what happens when your tidal volume falls in pressure-regulated volume control? The pressure goes up! The ventilator automatically increases the pressure, so then it's not really pressure control any more. It's not strictly pressure-limited, because you have the feedback loop in it. There are no "free lunches."

I agree with Dave: you have to know what you are dealing with, you have to know what to monitor, and you have to be prepared to adjust, realizing that as the pulmonary mechanics change, things on the ventilator change, and you need to respond. You respond to different things in volume control than in pressure control, but you need to respond.

Medoff: I agree. You really have to be there to manage these patients and see the changes.

Sorkness: Are there differences in treatment philosophy for adults versus pediatric patients?

Medoff: Since this is based on physiology, I guess it would depend on the physiologic differences between infants and adults. If the mechanics are the same, it should be the same approach for kids. Kids will probably tolerate some things better, such as hemodynamics. For instance, you'll probably worry less about the effects of intravenous epinephrine with regard to coronary disease. But the stakes are higher also, so it's always a little more nerve-wracking.

Colice: You can administer epinephrine; that's not a problem, but the benefit from ß agonists at that point (we've already seen the pathology) will be minimal.

Medoff: I have had some people turn around pretty nicely with intravenous epinephrine.

MacIntyre: We have so much angst about pushing albuterol, but nobody seems to care about giving intravenous epinephrine.

Sorkness: I think there are some data on anaphylaxis with intravenous epinephrine that suggest "buyer beware." There are dangers if you don't dilute the drug. Wrong doses are consistent with some toxicities.