Beyond the guidelines: Management of near fatal asthma

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Running head: Near fatal asthma
According to the national health interview survey of 2006, approximately 14% of American children have been diagnosed with asthma at sometime in their life (1). Nearly 5,000 people die each year in the US with asthma reported as their underlying cause of death. In children, asthma is often an allergic disease with exacerbations triggered by exposure to irritants such as tobacco smoke allergens, and infections, most often viral. The result of these exposures can be cumulative as well as synergistic. The severity of an exacerbation depends on the duration and quantity of the exposure, the child’s immune response to the trigger, and the availability and appropriate use of asthma medications.

Severe life threatening asthma and fatal asthma are often preventable. Reducing exposure to allergens and irritants, frequent monitoring of disease severity with early intervention when needed, and the appropriate use of medications such as inhaled corticosteroids (ICS) can dramatically decrease the risk of death from asthma. Using the Saskatchewan Health database, Suissa and colleagues have shown that in patients with asthma prescribed ICS, the risk of dying from asthma is decreased as they take more of their ICS as prescribed (2). It has also been shown that the risk of a severe asthma exacerbation requiring intervention with oral corticosteroids is inversely proportionate to the degree of adherence with ICS therapy (3).

Contributing factors to severe asthma include inadequate use of medications, poor access to medications and medical care, and a chaotic household (4). Household disorganization increases the likelihood of exposure to aero-irritants and allergens while decreasing medication adherence. Severe and fatal asthma has also been associated with
psychiatric disease in patients and in their caregivers. Presumably this decreases adherence and the likelihood of seeking help.

Patients with chronic severe asthma may have airway remodeling putting them at risk for baseline low lung function and a lesser degree of reversibility with inhaled beta agonist bronchodilators. These patients with chronic disease are also at risk of having blunted recognition of an asthma exacerbation. If breathlessness is one’s normal state, it can be difficult to recognize when additional therapy may be needed. There are a number of other reasons why adults and children with severe asthma may be non-adherent to their therapy (5).

Near fatal asthma is associated with air hunger and progressive hypoventilation with an increase in pCO2 resulting from hyperinflation and mismatch of ventilation and perfusion. Patients with dyspnea breathe at higher lung volumes while at the same time ineffectively ventilating large portions of their lung. Although bronchospasm related to smooth muscle contraction plays a role in this; mucus hypersecretion, airway obstruction, airway inflammation, and vascular leak are more likely to be far more significant causes of respiratory failure. It is common practice to give large doses of inhaled bronchodilators to treat severe acute asthma but there are few controlled clinical trials that suggest that this may be more effective than intermittent lower dose of beta agonist. Beta receptors are down regulated and rapidly saturated with the use of inhaled high dose beta agonist and although beta receptors may be up regulated following the use of corticosteroids, prolonged and high dose beta agonists are likely to carry greater risk than using a lower dose. These risks include tachycardia, hypokalemia, dysrhythmia, hypoglycemia, and increased mucus secretion. Similarly the systemic use of beta agonists should be avoided.
as this has no benefit over aerosol administration and carries substantially increased side effects.

Although there are data suggesting benefit to the concomitant use of an inhaled anticholinergic for treating acute severe asthma, a meta-analysis failed to show benefit when anticholinergic drugs were added to beta agonist for the therapy of life-threatening asthma (6). Data do not support the use of methylxanthines in acute severe or life threatening asthma.

Anti-inflammatory therapy is extremely important for the treatment of asthma. Typically oral or intravenous corticosteroids have been given at a dose of 2 mg/kg as frequently every 6 hours. There are no data that show that doses greater than 2 mg per kilogram per day or 80 mg for an adult are more effective than giving higher doses. Furthermore there are no data that show that giving therapy more frequently than every 12 hours has any benefit. Conversely, there are data suggesting that a significant number of patients who die suddenly from asthma have evidence of adrenal suppression (7). While it is common to discontinue ICS in patients with acute severe asthma, some data that suggest that concomitant use of ICS along with systemic steroids may provide additional benefit. At the very least this reinforces the importance of continuing to use ICS for patients with chronic severe asthma as the inadequate use is associated with asthma severity and exacerbations. Although corticosteroids are often administered intravenously, there are no data showing that this is more effective than oral medications.

Other medications that have been used for acute severe asthma include magnesium. Magnesium is safe, and a meta-analyses has shown that when given systemically it confers some additional benefit in the treatment of life threatening asthma
(8). Inhalation of a helium/oxygen combination (heliox) reduces the viscosity of the
inhaled gas and while this decreases work of breathing heliox is expensive and
administration of aerosols using heliox requires a different nebulizer system than that
used when driven by air (9).

Mechanical ventilation is often considered as a last resort in the treatment of
patients with life threatening asthma. In the patient with hyperinflation and gas trapping
mechanical ventilation can exacerbate ventilation-perfusion mismatch and air tapping,
risking air leaks such as pneumothorax. For these reasons if mechanical ventilation is
required, it is recommend that low or no end expiratory pressure be used, that there be a
significantly long expiration time and slow breathing rate to allow clearance of gas from
airways with long time constants, and that effective tidal volume be minimized both to
prevent volume trauma prevent auto-PEEP (10). Ventilator flow graphic monitoring can
be helpful in evaluating the stiffness of the lungs and the response to the different
pressures and volumes to recruit lung volume.

Patients who die of asthma usually have severe airway mucus obstruction and
literally drown in their secretions (11). There is evidence that this is associated with
abnormal mucin structure (12) and surfactant breakdown due to secretory phospholipases
(13). However, there is no proven role for the use of mucolytics in the treatment of
patients with acute life threatening asthma.

There are several identified genetic risk factors associated with severe asthma
including polymorphisms such as ADAM33 or the Arg/Arg phenotype of the beta agonist
receptor that have been associated with more severe asthma, or worsening disease control
with the use of long acting beta agonists (14).
Although asthma is generally an eosinophilic inflammatory disease a number of patients, especially those with steroid-dependent or steroid-resistant asthma have significant neutrophilic inflammation. It is been shown that corticosteroids induce apoptosis of eosinophils while prolonging neutrophil survival and this may be associated with a neutrophilic inflammation. It is also been thought that neutrophilic inflammation may be due to chronic airway infection with organisms such as mycoplasma or chlamydia. Macrolides used as immunomodulatory drugs that can reduce neutrophilic inflammation can be quite effective in decreasing asthma severity and the need for corticosteroids (15). These drugs have not been prospectively studied in treating life-threatening asthma.

Asthma is best treated before the episode ever becomes life threatening. Fortunately, most life threatening asthma attacks can be completely prevented by frequent patient monitoring and assessment, careful and accurate patient education and appropriate use of asthma medications(16).
References


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