Management of Status Asthmaticus in the Pediatric Intensive Care Unit: Review of Literature
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Received: 7-Apr-2015/Accepted: 14-Apr-2015/Published online: 15-May-2015

ABSTRACT
Asthma continues to be a chronic illness affecting millions of children worldwide. In spite of very good controller medications now available, Status Asthmaticus is one of the most common diagnosis among children admitted to the Pediatric Intensive Care Units. There are also a very wide variety of therapeutic options available to the intensivist for treating an asthma exacerbation. Although in conditions of extremes, probably it is worth to utilize all the therapies possible, more often than not, a practitioner has to choose one vs the other. In view of potential side effects of all the therapies, it is valuable to understand the evidence behind them. In this brief review we have tried to summarize the options and the research behind them.

Key words- Pediatrics, Status Asthmaticus. Asthma, Evidence-Based Medicine.

Acute severe asthma or Status Asthmaticus (SA) is an acute exacerbation of asthma that is unresponsive to initial standard treatment with short acting bronchodilators, anticholinergic drug, and corticosteroids. Approximately 25.9 million Americans (including 7.1 million children) had asthma in 2011; a rate of 84.8 per 1.000 population. The highest prevalence rate was seen in those 5-17 years of age (105.5 per 1,000 population). Status asthmaticus is one of the leading causes of hospitalization among children younger than 15 years in the United States. Asthma accounts for 29% of total pediatric hospital discharges, and in 2009, 157 deaths of patients younger than 15 years were attributed to asthma. Morbidity and mortality from asthma are decreasing as a result of the multiple modalities for intervention available in the emergency department, general pediatric floor, and intensive care unit. Because asthma has the highest morbidity rate of all pediatric diseases, it has been widely studied around the world. However, as with most diseases in modern medicine, some dogmas and therapies are unsubstantiated by any evidence-based research. Exemplifying the large variations in asthma management is a multicenter study by Bratton et al. that took place over 3 years and included 7,125 children: rates of invasive mechanical ventilation (MV) use in patients with SA varied from 6% for those admitted to a pediatric intensive care unit (PICU) in the Pacific region to 27% in the East North Central region. Therapeutic intervention varied widely by census region, with 26% receiving systemic β-agonists, 59% inhaled anticholinergics, 21% magnesium sulfate, 6% methylxanthines, 10% inhaled helium-oxygen gas mixtures, and 14% endotracheal intubation and MV.

In this review article, we aimed to identify the evidence for various therapeutic options available to treat SA in children, from the emergency room to the intensive care unit. Independent literature searches (using PubMed and Google Scholar) were conducted by 2 of the authors (S.T. and G.C.) to identify studies regarding various therapeutic options for severe asthma. Recently published meta-analyses and systematic reviews were also included in the search. Studies that were deemed relevant by both investigators were included in this review. We did not attempt to conduct a systematic review or a meta-analysis of published studies, but this review represents a compilation of prior research pertinent to clinicians caring for children with acute severe SA. Each type of therapy is discussed in the following sections followed by the practice followed by our standard practice (in italics) and a decision support algorithm (Figure 1).
Sympathomimetic (β2-Agonist) Therapy
Bronchodilation by β2-agonist therapy has been the cornerstone of acute asthma therapy for both outpatients and inpatients. Although its effectiveness is not debated, some unresolved questions remain related to the different agents, doses, and routes of administration.

Continuous Albuterol
Nebulized albuterol 2.5 mg every 1 to 2 hours is effective in decreasing asthma symptoms rapidly. Continuous delivery of nebulized albuterol is routinely used in emergency departments and intensive care units. There is some evidence in favor of using continuous therapy vs hourly therapy in severe asthma. In a randomized study of 17 pediatric asthma patients, with 1 group receiving 0.3 mg/kg per hour of continuous albuterol and the other group receiving 0.3 mg/kg over 20 minutes every hour, Papo et al4 found that the patients in the continuous albuterol group improved quicker and had a shorter duration of hospital stay. Continuous albuterol in doses ranging from 5 mg/hour to 20 mg/hour is routinely used as a first line agent.

Metered-Dose Inhaler
A metered-dose inhaler (MDI) is an effective and efficient mode of delivering aerosolized medication to the respiratory tract. MDI with a valved holding chamber works very well even in small children, who can have increased anxiety with nebulizations. The MDI/valved holding chamber drug delivery system offers a shorter treatment time, does not require electricity, and is more effective than use of a nebulizer in young children in the emergency department setting5. The widespread perception that nebulization is somewhat more effective is not supported with evidence. In a single-blind, prospective randomized trial6, patients aged 1 to 24 months with moderate to severe wheezing were randomly assigned to receive either MDI with a spacer (2 puffs, 100 mcg each, every 10 minutes for 5 doses) or nebulizer treatment (0.25 mg/kg every 13 minutes for 3 doses). Treatment success, as defined by a clinical score of less than 5 (Score range 1-12, with higher score for more severe asthma), was 90% in the MDI group vs 71% in the nebulizer group (P=.01) after the first hour. The MDI/valved holding chamber may be better tolerated and achieve similar if not better drug delivery than compared with nebulization.

Levalbuterol
Levalbuterol (Xopenex, Sunovion Pharmaceuticals Inc), an orally inhaled racemic albuterol, has the theoretical advantage of causing less tachycardia. It is therefore widely prescribed in small children. However, independent clinical trials have mostly been unremarkable. A 2009 double-blind, randomized controlled trial (RCT) of high-dose continuous albuterol vs racemic albuterol in 81 children aged 6 to 18 years showed similar time requirements for both therapies, as well as similar changes in heart rate7. A study measuring changes in clinical asthma scores and forced expiratory volume in 1 second (FEV1) changes also showed no difference8. Levo-albuterol is significantly more expensive than racemic albuterol and may offer no advantage during the initial asthma exacerbation treatment.

Subcutaneous Adrenergic Agents
Epinephrine is a nonselective adrenergic agent, but α action predominates at higher doses and β1/β2 at lower doses. Subcutaneous or intra muscular use of epinephrine has been used for management of acute severe asthma. Studies, however, have not shown a conclusive difference in outcomes comparing subcutaneous epinephrine with nebulized albuterol9. Terbutaline is a β-selective adrenergic agent, although it loses its β2-selective property when administered subcutaneously, and offers no advantage over epinephrine.10 However, 1 double-blind crossover study comparing 0.25 mg of epinephrine with 0.5 mg of terbutaline showed a more pronounced effect with regard to forced vital capacity, FEV1, maximal expiratory flow rate, and maximal midexpiratory flow rate in the group who had received terbutaline11. Single administration of I.M terbutaline in the emergency department and in the PICU is utilized for impending respiratory failure to potentially
avoid intubation and to allow steroids and nebulized albuterol to take effect.

Continuous Terbutaline Infusion
A severe asthma exacerbation leads to impaired delivery of nebulized medications to the tracheobronchial tree, with resulting limited therapeutic effect. A β-selective bronchodilator given systematically has a potential advantage in such circumstances, with intravenous (IV) terbutaline infusions being the preferred agent by most emergency department physicians and intensivists. The clinical benefit of continuous terbutaline and its safety profile has been shown to be favorable in small nonrandomized trials12 and retrospective studies13. However, a prospective, randomized, double-blind trial failed to show clinical benefit after adding IV terbutaline to the treatment regimen of children aged 2 to 17 years who were already receiving continuous high-dose albuterol. Specifically, no difference was observed in clinical asthma severity scores, number of hours on continuous albuterol, or PICU length of stay between the group receiving IV terbutaline plus albuterol vs albuterol alone14.

Terbutaline infusion is the preferred second line agent for failure to respond to nebulized albuterol/steroids.

Anticholinergic Agents
Ipratropium bromide (Ipravent; Cipla) is an anticholinergic agent that acts by inhibiting parasympathetic-mediated bronchospasm. Used alone or in combination with albuterol, it is a popular first-line therapy for management of asthma in children in the emergency department. The clinical studies regarding its usage have been equivocal. RCTs by Craven et al15 and Goggin et al16 have shown no benefit of adding ipratropium bromide to a standard regimen of albuterol and corticosteroids, as measured by asthma score, hospital length of stay, or changes in FEV1. However, in a larger trial of 434 children by Qureshi et al17 the subset of patients with more severe asthma had significantly decreased need for hospitalization with the addition of ipratropium bromide.

Ipratropium given in combination with albuterol (Combi-nebs) is used frequently in the ED setting, however due to limited data on efficacy in PICU patients not used routinely in the PICU.

Corticosteroids
Corticosteroids, along with nebulized albuterol, are considered the standard initial therapy for asthma. Multiple trials have documented the efficacy of corticosteroids, but variations in agents, doses, and routes of administration persist. Many studies have shown equal efficacy of oral vs IV corticosteroids18. A Cochrane review in 2000 identified 7 trials with a total of 426 children treated with IV/oral or nebulized corticosteroids19. The authors concluded that some forms of systemic corticosteroids (oral or IV) decreased hospital length of stay, and these patients were less likely to have a relapse within 3 months. Inhaled corticosteroids were not found to be equivalent to systemic corticosteroids for treatment of acute asthma exacerbations in this review19. Other trials have shown no benefit in outcomes using high-dose corticosteroids compared with “standard” doses16, 17. In fact, a single dose of intramuscular dexamethasone has been found to be equally efficacious to a 3-day oral prednisolone course when comparing clinical improvement and prevention of further emergency department visits20.

Ipratropium bromide (Ipravent) is used frequently in the E.D setting, however due to limited data on efficacy in PICU patients not used routinely in the PICU.

Magnesium Sulfate
Magnesium sulfate 25 mg/kg over 20 minutes during the first hour of an asthma exacerbation is a second-line agent that has been shown to significantly decrease the need for mechanical ventilation in pediatric patients, 2-15 years old31. Magnesium sulfate produces bronchodilation by relaxing smooth muscles. However, its bronchodilation efficacy is variable. Some patients show vigorous response to magnesium sulfate, and others are virtually
unresponsive. This may be due to variations in the severity of asthma. Studies have been equivocal, although more data support the use of magnesium. Noppen et al\textsuperscript{22} in 1990 showed significant improvement in pulmonary function tests and clinical status with use of IV magnesium in a small group of 12 patients with severe asthma. Another RCT in 1996 showed a greater percentage of improvement in FEV\textsubscript{1} with use of IV magnesium infusion compared with placebo\textsuperscript{23}. However, in a subsequent RCT, a single dose of 75 mg/kg of magnesium sulfate did not show any advantage as a treatment adjunct\textsuperscript{24}. Magnesium should be employed during the first hour of asthma exacerbation treatment in patients who demonstrate poor improvement in SpO\textsubscript{2}, cyanosis, use of accessory muscles, expiratory wheezes, and level of consciousness.

Methylxanthines
Theophylline was once the standard pharmaceutical agent for treatment of acute asthma. However, with its narrow therapeutic index and availability of safer agents, its use has declined in developed countries. Theoretically, with careful monitoring of drug levels, aminophylline may be as safe as any b-agonist. An RCT from 1998 by Yung and South\textsuperscript{25} showed greater improvement in spirometry at 6 hours, higher oxygen saturations in 30 hours, and a significant decrease in intubation rates using theophylline combined with terbutaline compared with terbutaline alone. This study included 40 children aged 3 to 15 years with impending respiratory failure. Similar results were observed by Wheeler et al\textsuperscript{26} in a more recent trial, which also showed decreased length of stay and incidence of adverse events with aminophylline compared with terbutaline. A Cochrane review\textsuperscript{27} failed to show a decrease in symptoms, number of nebulization treatments, or length of stay (LOS) with aminophylline. However, that review also showed that the addition of aminophylline to standard therapy with \(\beta\textsubscript{2}\)-agonist and corticosteroids significantly improved FEV\textsubscript{1} after 6 to 8 hours and peak expiratory flow rate at 12 to 18 hours. Although aminophylline was well tolerated, the treatment group had a significantly increased incidence of vomiting. An expert panel commissioned by the National Asthma Education and Prevention Program (NAEPP) does not recommend methylxanthines in the emergency care or hospital setting\textsuperscript{28}. Due to safer alternative agents, no significant improvement in symptoms, no decrease in LOS, and limited supply, methylxanthines are not recommended in the PICU setting.

Heliox
Substitution of nitrogen with helium in the inspired air (heliox) decreases the density of gas, which in turn makes the flow of gas through a circular tube (ie, tracheobronchial tree) easier. Heliox produces a marked response in children with upper airway obstruction and croup. Its use in asthma, however, has only been studied in small trials and has had conflicting results. One prospective trial in 11 children aged 5 to 18 years showed no significant difference in clinical score or spirometry at baseline and 15 minutes after initiation of a 70% helium/30% oxygen gas mixture\textsuperscript{29}. However, Kudukis et al\textsuperscript{30} showed lower peak flow and lower dyspnea index in an RCT of 18 patients aged 16 months to 16 years with longer use of heliox gas mixture. Another study reported the successful use of heliox to improve ventilation in 28 intubated children with asthma.\textsuperscript{31} However, a rather large RCT involving the use of heliox in 42 children aged 2 to 21 years with moderate to severe asthma failed to show any difference in clinical asthma score or PICU or hospital length of stay\textsuperscript{32}. Not routinely used. Occasionally tried in refractory patients who do not have oxygen requirement.

Antibiotics
Asthma is a mechanical event, triggered by the hypersensitivity of the musculature in the bronchial wall. It has been proposed that infections may exacerbate such acute episodes. There are strong arguments in favor of an association between atypical bacteria (Mycoplasma or Chlamydia) and asthma in school-aged children\textsuperscript{33}, which has generated interest in the use of azithromycin in acute asthma episodes. The anti-inflammatory properties of azithromycin are also believed to help control asthma exacerbations\textsuperscript{34}. 

Due to safer alternative agents, no significant improvement in symptoms, no decrease in LOS, and limited supply, methylxanthines are not recommended in the PICU setting.
There are no large studies documenting the efficacy of azithromycin in children, but some evidence in the adult literature supports the efficacy of macrolide antibiotics. In an RCT in 278 adults with asthma, patients randomly assigned to receive telithromycin within 24 hours of an acute exacerbation had a significantly greater decrease in asthma symptoms than patients assigned to receive placebo. This study also showed that identification of M pneumonia and C pneumonia by polymerase chain reaction in asthmatic patients best identifies the macrolide-responsive phenotype. Similar use of amoxicillin in an RCT among adult patients with asthma did not show a beneficial effect.

The decision to start antibiotics for comorbid conditions based on the intensivists judgment.

Ketamine
Ketamine is a synthetic derivative of phencyclidine and is often recommended as the induction agent for the asthma patient because of its bronchodilatory properties and sedative effects. Ketamine has been administered as a continuous infusion for sedation in patients receiving invasive or noninvasive positive pressure ventilation for asthma. It is also used to break refractory bronchospasm in intubated patients. Some prospective trials and case reports suggest that it may be a useful adjuvant to standard therapy in children with impending respiratory failure. In a prospective observational study in the emergency department, Pettrillo and colleagues administered ketamine as an infusion to 10 nonintubated patients who were unresponsive to standard therapy for asthma. They showed a significant improvement in asthma scores and oxygen saturations.

Ketamine is used for, a) Induction for intubation, b) Sedation for intubated asthmatics, c) Light sedation for small children who do not tolerate CPAP/BiPAP.

Chest Physiotherapy and Airway Clearance
Chest physiotherapy (CPT) can theoretically augment airway clearance and encourage resolution of mucus plugging. Some clinicians recommend CPT for asthma, although no clinical studies have evaluated its effect. In a hyperinflated chest, CPT may be harmful by increasing the risk of pneumothorax. The only instance in which it may be helpful is in small children with clear segmental or lobar atelectasis. The argument can be made that CPT is helpful in infants with bronchiolitis, but evidence for its utility in bronchiolitis is not very strong. In fact, a recent meta-analysis of 3 RCTs found no benefit of using CPT with vibration or percussion techniques in children younger than 24 months. A small percentage of patients with asthma on MV may require and can benefit from selective suction of mucus plugs/casts or thick secretions by bronchoscopy. For most exacerbations, chest physiotherapy is not beneficial and is unnecessarily stressful for the breathless asthma patient.

Chest physical therapy is not generally recommended.

Oxygen
All patients with asthma have ventilation-perfusion ratio mismatch and require some supplemental oxygen. It is important to remember that albuterol induces bronchodilation and, as a result, decreases hypoxic vasoconstriction and worsens hypoxemia, therefore increasing ventilation-perfusion ratio mismatch. Because of the potential for hypoxia, the recommended driving gas for albuterol nebulization is oxygen. In a randomized crossover study that included 27 episodes of acute asthma exacerbation, the effect of oxygen as a driving gas was noted to be transient. In adult patients with chronic obstructive pulmonary disease, there is a concern for suppression of hypoxic respiratory drive with supplemental oxygen; this phenomenon is not seen in otherwise healthy children with asthma. In adult patients with asthma, 100% oxygen administration has also been found to adversely affect gas exchange. In a trial of 37 adult patients with asthma, Chien et al. observed an increase in PaCO2 between 1 and 10 mm Hg within 25 minutes of 100% oxygen administration. No such trial has been conducted in pediatric patients. Utilized as needed to maintain saturations above 90% and less than 98%.

Fluids
Most asthmatic children are dehydrated at initial
evaluation (poor fluid intake, vomiting, increased insensible fluid losses from the respiratory tract). Dehydration produces thicker, more tenacious bronchial secretions, thereby leading to worsening bronchial mucus plugging. Fluid replacement and maintenance of euvolemic state are necessary to minimize thickening of secretions. It is common for children admitted for severe asthma to receive fluid boluses and to be started on maintenance IV fluids. However, caution is advised regarding fluid therapy in asthmatic patients because of the risk of SIADH (syndrome of inappropriate antidiuretic hormone) and consequent hyponatremia and fluid overload42.

SA is associated with high negative transpulmonary pressures; this facilitates fluid accumulation around respiratory bronchioles and thus leads to pulmonary edema and decreased respiratory status43. No studies have evaluated a conservative vs liberal fluid strategy in the management of asthma. Corrections of fluid status should be guided by serial assessment of urine output, urine specific gravity, mucus membrane moisture, and serum electrolytes.

Intravenous fluids (0.45 NS) should be given at a rate to ensure an acceptable fluid status in children who are not able to tolerate oral rehydration. Serum electrolytes should be obtained on admission.

Chest Radiography

Chest radiography (CXR) is frequently performed for children with asthma exacerbation. Children with persistent hypoxemia despite therapy are at higher risk for abnormalities on CXR. Tsai et al44 prospectively compared CXR findings in hypoxemic vs nonhypoxemic children aged 1 to 17 years. They found both small and large lung volumes, extravascular fluid, and atelectasis to be more common in radiographs from hypoxemic asthmatic patients. However, they found no correlation between CXR findings and duration of hypoxemia, hospital stay, or PICU admission. Significant findings on CXR are relatively rare, as shown by Brooks et al45, who found significant abnormalities in only 7 of 128 children with acute asthma. The CXR findings commonly observed are lung hyperinflation, hypoinflation, or atelectasis. Lung hypoinflation is considered a sign of respiratory fatigue and poor prognosis and has been associated with a greater likelihood of hospital admission in children aged 6 years or older46.

If not obtained in the E.D, all asthmatics requiring admission to the PICU should have a CXR acquired to assess for pneumothorax, pneumomediastinum, pneumonia, or atelectasis.

Noninvasive Ventilation

The presence of air trapping in acute asthma exacerbation leads to auto–positive end expiratory pressure, which requires the patient to generate higher negative inspiratory pressures to overcome it. The use of continuous positive airway pressure allows for equilibration of pressure between the mouth and alveoli and can facilitate better gas exchange and decreased work of breathing. The use of noninvasive ventilation (NIV)—continuous positive airway pressure and biphasic positive airway pressure (BiPAP)—has gained acceptance in managing difficult-to-control asthma, especially as a temporizing measure while awaiting therapeutic benefit of pharmacotherapy. The safety and efficacy of BiPAP in asthma has been demonstrated by many retrospective studies in the PICU47 and in the emergency department48.50. Thrill et al51 conducted a prospective study with a crossover design in 20 children. They placed children on BiPAP for 2 hours, followed by conventional treatment for 2 hours, or vice versa. They found significant decreases in both respiratory rate and clinical asthma score at the end of the 2 hours on BiPAP. A 2012 prospective RCT that randomly assigned 20 patients to either NIV or standard therapy showed significant improvement in clinical asthma scores at 2 hours, 4 to 8 hours, 12 to 16 hours, and 24 hours after initiation of BiPAP (P< .01)52. No major adverse events related to NIV occurred.

Commonly used as a second line agent for children who can tolerate. May need to use sedation (ketamine or dexmedetomidine).

Invasive Mechanical Ventilation

The indications to intubate patients with asthma include hypoxemia despite high concentration of oxygen on NIV, severely increased work of breathing,
altered mental state, or cardiac arrest. Hypercarbia alone is not an indication for intubation, although progressively increasing PaCO₂ despite maximal therapy warrants intubation. Managing asthma in children on MV is very challenging. Despite decades of experience, an optimal strategy has not been established. In 1984, Darioli and Peretti introduced the concept of permissive hypercarbia in adult asthma and showed that an MV protocol to manage hypoxemia, without attempting to restore adequate alveolar ventilation, is safe. In addition, the risks of barotrauma and circulatory failure, which are frequently reported as fatal complications, appear to be significantly decreased with this strategy. Successful management of asthma with PaCO₂ up to 269 mm Hg has been described. Trials of different modes of MV in the pediatric population are scarce. To ensure minute ventilation, volume control ventilation is considered standard. Sarnaik and colleagues, however, published a retrospective review of 40 children who were successfully ventilated with a pressure-control mode using an inspiratory-to-expiratory time ratio of 1:4 with the pressure adjusted to target an exhaled tidal volume of 10 to 12 mL/kg. The pressure-control mode can be a safe and effective mode of MV in acute asthma. Intubation is avoided if possible. No one mode has been shown to be better than the other. Ventilator settings (PEEP, I:E ratio, Rate and Tidal volume) need fine adjustment to meet individual patient requirements. Permissive hypercapnia practiced if pH can be maintained above 7.2.

Tracheal Gas Insufflation
Tracheal gas insufflation (TGI) as an adjuvant to MV delivers fresh gas into the central airways continuously or in a phasic manner to improve efficiency of alveolar ventilation or to minimize ventilator pressure requirements. Recently, TGI has received attention as an ideal lung-protective strategy for MV. Human studies on TGI are lacking, although animal experiments are promising. Eckmann, in 2000, published a prospective trial on the use of chest wall vibration along with TGI during experimental bronchoconstriction in 6 anesthetized dogs. He showed that gas exchange was achieved in the TGI group at lower airway and intrathoracic pressures than those receiving standard MV. If obstacles to clinical implementation of TGI can be overcome, it may lead to the development of commercial systems with widespread TGI application. Not routinely used.

Anesthetic Gases
Inhalational anesthetics (halothane, isoflurane, and sevoflurane) are potent bronchodilators. Although the mechanism of action of inhalational anesthetics is unknown, their use in animal models and case reports of patients with respiratory acidosis has resulted in improved ventilation. Practical limitations to the use of inhalational anesthetics include the abrupt return of bronchoconstriction after discontinuation and the need for delivery via an anesthesia machine, with proper scavenging of the anesthetic gases. Nevertheless, their use has been tried as a rescue maneuver in children with acute severe asthma exacerbation with persistent ventilatory failure despite appropriate MV and aggressive medical therapy. The largest pediatric case series on the use of isoflurane for SA reported on 6 children aged 14 months to 15 years in whom conventional treatments had failed. A standard protocol was used for management in all patients (initiation with 1%-2% isoflurane, increased by 0.1% every 15 minutes until therapeutic effect), which resulted in statistically significant improvements in PaCO₂, peak inspiratory pressure, and pH. All 6 patients were successfully treated and discharged from the hospital without sequelae. Utilized in refractory conditions. Anesthesia machine needs to be brought in the PICU and managed in conjunction with the anesthesia.

High-Frequency Oscillatory Ventilation
High-frequency oscillatory ventilation is an accepted management technique for pediatric respiratory failure. It is generally contraindicated in obstructive airway disease, however, because of the risk of air trapping. As opposed to conventional ventilation, high-frequency oscillatory ventilation has an active expiratory phase, which may account for reports
of its successful use in children with asthma. It is essential to apply sufficient mean airway pressure to open and stent the airways and to use lower frequency to overcome the greater attenuation of the oscillatory waves in the narrowed airways. As in conventional ventilation, permissive hypercapnia is a desirable strategy. Reserved for refractory cases who may not be suitable candidates for extra corporial support.

**Extracorporeal Membrane Oxygenation**

With the many excellent management options available, use of extracorporeal membrane oxygenation (ECMO) for pediatric SA is rarely required, although some case reports have described successful use of ECMO in refractory hypercapnic respiratory failure. A single-center experience with the use of ECMO in 13 children from 1986 to 2007 reported 100% survival and no neurologic sequelae. The extracorporeal life support registry during that time frame had 51 children placed on ECMO for SA, with 94% survival. Pumpless arteriovenous CO₂ removal is being increasingly used in adults for hypercapnic respiratory failure in chronic obstructive pulmonary disease. Due to vessel size limitations, percutaneous cannulation in children is difficult, but some case reports have described its successful use in children as young as 4 years.

**Refractory cases. With more experience on anticoagulation and single lumen access cannula, we believe we would be utilizing extra corporeal support earlier and more frequently in future.**

**Conclusions**

Despite an elaborate arsenal available, management of refractory SA can be a daunting task for a physician. Excellent best practice recommendations have been published by the National Asthma Education and Prevention Program. These guidelines give expert panel opinion for stepwise management of SA. We believe that this review can help clinicians understand the evidence behind the recommendations, as well as the research on the options for refractory SA. Further research is needed on these modalities, especially modes of ventilation (invasive and noninvasive) and extracorporeal support for refractory hypercapnia.

**Conflict of Interest:** None  
**Source of Funding:** None

**References**

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Jun;23(6):355-61.
34. Johnston SL., Blasi F, Black PN, Martin RJ, Farell DJ, Nieman RB. The effect of telithromycin in acute exacerbations of asthma. NEJM 2006;354:1589-1600.


