

Successful Treatment of Acute Chest Syndrome With High-Frequency Oscillatory Ventilation in Pediatric Patients

Angela T Wratney MD, Michael A Gentile RRT, Donna S Hamel RRT,
and Ira M Cheifetz MD FAARC

Severe acute chest syndrome afflicts patients with sickle cell disease and can cause hypoxemia refractory to conventional treatments. Obstructive mucus plugging and the development of acute respiratory distress syndrome may underlie the pathophysiology of refractory hypoxemia in acute chest syndrome. Although high-frequency oscillatory ventilation (HFOV) is well established in the treatment of pediatric acute respiratory distress syndrome, there is no support in the literature for its role in managing hypoxemia in acute chest syndrome. In disease processes with high airways resistance and obstructive mucus plugging, HFOV may predispose to air-trapping and increased morbidity secondary to air leak syndromes. We report the first successful HFOV management of pediatric patients suffering from severe acute chest syndrome and hypoxic respiratory failure. These cases suggest that HFOV should be strongly considered for patients with severe acute chest syndrome that is refractory to conventional mechanical ventilation. Key words: acute chest syndrome, sickle cell anemia, pediatric, acute respiratory distress syndrome, acute lung injury, mechanical ventilation, high-frequency ventilation, hypoxia. [Respir Care 2004;49(3):263–269. © 2004 Daedalus Enterprises]

Introduction

Acute chest syndrome (ACS) occurs in patients with sickle cell disease and is classically characterized by fever, pleuritic chest pain, tachypnea, cough, hypoxemia, marked leukocytosis, and diffuse infiltrates on chest radiograph.^{1–3} This syndrome more commonly occurs during childhood in patients with HbSS red blood cells (classic sickle cell anemia).¹ However, ACS can be associated with other forms of sickle cell disease, including Sickle- β^o thalassemia and HbSC (sickle-hemoglobin C disease).

ACS is the leading cause of hospitalization in sickle cell disease patients, accounting for 12–15% of hospital admissions.^{1,4–6} ACS accounts for 30% of deaths in children with sickle cell disease < 10 years old and is the single

most common cause of death in those > 10 years old.^{7,8} Overall, ACS episodes are associated with a mortality rate of 10–12%.^{5,9,10} The mortality of ACS patients who require intubation for respiratory failure is unknown, but in the landmark study by Vichinsky et al, which analyzed the causes and outcomes of ACS in 538 pediatric and adult patients, 13% of the patients required mechanical ventilation and 3% died.⁹

One of the clinical hallmarks of severe ACS is refractory hypoxemia, which may result from (1) microvascular occlusion due to sickled erythrocytes and increased adhesion of red blood cells to the vascular endothelium,¹¹ (2) disturbance of endothelial vasoactive mediators,¹² (3) release of inflammatory cytokines due to infection or vascular injury,¹³ (4) activation of the coagulation cascade system,^{14,15} (5) fat embolism from bone marrow infarction,¹⁶ and (6) exaggerated regional hypoxic pulmonary vasoconstriction.¹⁷ Hypoxia may also result from inspissated secretions within the airways, leading to severe ventilation-perfusion mismatching. A very severe form of mucus obstruction, termed “plastic bronchitis,” is well documented in ACS patients.^{18–21} These mucus casts may become firmly wedged in the airways and occlude the tracheobronchial tree at many levels.¹⁹ It remains unclear

Angela T Wratney MD, Michael A Gentile RRT, Donna S Hamel RRT, and Ira M Cheifetz MD FAARC are affiliated with the Division of Pediatric Critical Care Medicine, Duke Children’s Hospital, Duke University, Durham, North Carolina.

Correspondence: Angela Wratney MD, Division of Pediatric Critical Care Medicine, Duke University Medical Center, Box 3046, Durham NC 27710. E-mail: wratn001@mc.duke.edu.

whether the hypoxia associated with ACS is related primarily to airway plugging or to the development of acute parenchymal lung injury (ie, acute respiratory distress syndrome [ARDS]).

Conventional therapies for the prevention and treatment of ACS include bronchodilators, supplemental oxygen, incentive spirometry, exchange transfusions, analgesia, and aggressive treatments to mobilize and remove mucus. When these initial therapies fail, hypoxic respiratory failure requires mechanical ventilation. Some ACS patients may be managed with routine, or "safe," conventional mechanical ventilation (CMV) settings. However, patients with severe ACS and refractory hypoxemia may require potentially dangerously high CMV settings to maintain adequate lung aeration and oxygenation. Although high-frequency oscillatory ventilation (HFOV) is well established for the treatment of pediatric acute lung injury,²²⁻²⁴ there is no support in the literature for HFOV's role in managing severe ACS.²²

Theoretically, there is concern that HFOV may predispose to air-trapping and greater morbidity due to air leak syndromes in disease processes, such as ACS, that have high airways resistance and obstructive mucoid plugging. In our review of the literature we found no reports of successful use of HFOV for managing respiratory failure in severe ACS that required mechanical ventilation. This report describes 6 pediatric patients with severe ACS and hypoxic respiratory failure refractory to CMV who were successfully managed with HFOV. Procedures were conducted in accordance with the Declaration of Helsinki, and permission to report this series was granted by our institutional review board.

Case Reports

The presentation and management information of the 6 patients was obtained from a retrospective chart review (Table 1). Upon admission to the pediatric intensive care unit (PICU) each patient received a double-volume red blood cell exchange transfusion, performed to a goal of $\leq 30\%$ sickled hemoglobin. Additional therapies continued during the intensive care course included chest physiotherapy and suctioning as indicated, intravenous fluid administration at a maintenance rate, opiate analgesia, and antibiotic therapy with vancomycin, ceftriaxone, and azithromycin (except as indicated below). All patients received one or more of the following for adjuvant therapy: aerosolized albuterol, intratracheal N-acetylcysteine, dornase alfa, and/or intravenous methylprednisolone.

Patients were intubated based on standard clinical assessment and were initially ventilated with the Servo 300 ventilator (Siemens, Solna, Sweden). The use of the high-frequency oscillator (SensorMedics 3100A, Viasys Healthcare, Yorba Linda, California) was at the discretion of the pediatric intensivist but generally occurred when the pa-

Table 1. Patient Characteristics

Case Number	Age (y)	Sex	Weight (kg)	Total Duration of CMV (h)	Total Duration of HFOV (h)	Bronch* (No.)
1	6	M	26.6	222	96	2
2	5	F	24.3	259	132	8
3	5	M	20.0	102	90	4
4	7	F	29.4	50	130	5
5	6	M	27.0	186	48	3
6	12	M	36.3	46	108	1

CMV = conventional mechanical ventilation
HFOV = high-frequency oscillatory ventilation
*number of bronchoscopies performed for secretion clearance during mechanical ventilation

tient required two or more of the following CMV settings: positive end-expiratory pressure (PEEP) ≥ 10 cm H₂O, mean airway pressure (P_{aw}) ≥ 15 cm H₂O, peak inspiratory pressure (PIP) ≥ 32 cm H₂O, and/or fraction of inspired oxygen (F_{IO_2}) ≥ 0.60 . All patients were hemodynamically stable during and after transition to HFOV. Pharmacologic sedation and neuromuscular blockade was administered to all 6 patients during the transition from CMV to HFOV.

Bronchoscopy was performed at the discretion of the intensivist when a patient had persistent hypoxia, an inability to wean below an F_{IO_2} of 0.60, or tenacious secretions that were difficult to remove by routine endotracheal tube suctioning. Bronchoscopy was successfully performed during both CMV and HFOV. Each procedure was generally completed in 10–15 min. Normal saline, urokinase, N-acetylcysteine, and/or deoxyribonuclease lavage was employed to remove occlusive plugs. If the patient had a good clinical response (ie, improvement in chest radiograph, ventilator weaning, decreased F_{IO_2} , or improved clearance of mucoid secretions), bronchoscopy was repeated on sequential days until no further improvement was obtained. All patients tolerated bronchoscopy well, without the requirement for increased ventilator or hemodynamic support for any substantial length of time following the procedure. In many cases pulmonary compliance and oxygenation improved post-bronchoscopy, allowing weaning of the ventilatory settings.

Case 1. A 6-year-old boy with HbSS disease was transferred from an outside hospital because of worsening respiratory distress. Two days prior to transfer he had presented to the emergency department with a 3-day history of flank pain, fever, and cough. He had completed a 7-day course of erythromycin for an upper respiratory infection but complained of new right-sided chest pain and fever. His medical history included multiple admissions for pain crisis management, recurrent pneumonia, and reactive airway disease. At presentation his blood oxygen saturation

(measured via pulse oximetry) was 86% on room air and he had substantial retractions. Laboratory values included a hemoglobin of 6.1 g/dL and white blood cell count of 54,400 cells/ μ L (57% neutrophils, 2% bands, 10% lymphocytes, and 9% monocytes). The initial chest radiograph revealed diffuse bilateral parenchymal infiltrates and small bilateral pleural effusions. Despite bronchodilator therapy and analgesia, he required a nonrebreather mask and F_{IO_2} 1.0, and his respiratory status rapidly deteriorated. He was intubated prior to placement of a femoral venous catheter for erythropheresis.

Upon intubation, copious, tenacious secretions were suctioned from the endotracheal tube. His initial P_{aO_2}/F_{IO_2} ratio was 110 mm Hg, and the oxygenation index (OI = mean airway pressure \times F_{IO_2} \times 100/ P_{aO_2}) was 15. Maximal ventilator settings were reached after 30 hours on conventional ventilation: PIP 40 cm H₂O, PEEP 10 cm H₂O, F_{IO_2} 1.0 (OI 32). The resultant arterial blood gas (ABG) values were pH 7.25, P_{aCO_2} 61 mm Hg, P_{aO_2} 46 mm Hg. HFOV was initiated, and after 6 hours the \bar{P}_{aw} was 28 cm H₂O, amplitude pressure was 57 cm H₂O, respiratory frequency was 5 Hz, and F_{IO_2} was 0.80. ABG analysis revealed pH 7.41, P_{aCO_2} 39 mm Hg, P_{aO_2} 81 mm Hg, blood oxygen saturation 94%. OI had decreased slightly, to 28. Bronchoscopy was performed twice (once during CMV and once during HFOV) to assist in secretion removal and expansion of the atelectatic areas of lung visible on chest radiograph. After 96 hours on HFOV the OI had fallen to 11 and the patient was able to convert to CMV. He was successfully extubated 8 days later and discharged from the hospital 10 days after extubation, without the need for bronchodilator or oxygen therapy.

Case 2. A 5-year-old girl with HbSS disease and no history of respiratory complications was admitted after a 3-day history of right-upper-quadrant abdominal pain and a temperature of 38.9°C. Initial hemoglobin and white blood cell values were 6.5 g/dL and 34,800 cells/ μ L, respectively. The differential included 61% neutrophils, 2% bands, 26% lymphocytes, and 10% monocytes. Chest radiograph demonstrated small right middle and lower lobe infiltrates. In addition to erythromycin, antibiotic coverage for abdominal pathogens included ampicillin, gentamicin, and clindamycin. On her second hospital day she developed worsening respiratory distress, requiring F_{IO_2} 0.90. Chest radiograph revealed progression of the infiltrates and development of a large left-sided pleural effusion. Hemoglobin electrophoresis revealed 48% HbS phenotype cells and 52% HbA phenotype cells, with hemoglobin of 5.5 g/dL. She was transferred to the PICU, intubated, and administered a simple packed red blood cell transfusion. After placement of a pheresis line she received a double-volume exchange transfusion erythropheresis. A chest tube removed 300 mL of sterile exudate. After 46 hours of

CMV the F_{IO_2} remained at 0.85 and substantial pleural drainage persisted. The maximum CMV settings included PIP 34 cm H₂O, PEEP 12 cm H₂O, F_{IO_2} 0.85 (OI 35). Bronchoscopy was performed twice to remove thick, rubbery plugs from the right middle and lower lobes, but substantial obstructive plugging remained.

HFOV was initiated, with \bar{P}_{aw} 34 cm H₂O, amplitude 47 cm H₂O, and frequency 8 Hz. After 6 hours the OI decreased to 25. Subcutaneous air was noted on physical examination on day 2 of HFOV (\bar{P}_{aw} 28 cm H₂O). A small pneumothorax was identified on chest radiograph, which resolved with a minor adjustment of the existing chest tube. The patient suffered frequent episodic desaturations that were believed to be secondary to mucus plugging. Bronchoscopy was performed on 8 separate occasions (two during CMV, six during HFOV) eventually with the successful removal of thick mucoid secretions. Cultures of the bronchoalveolar and pleural drainage were negative for bacteria, fungus, and virus. After 6 days of HFOV the ventilation mode was converted to CMV, with PIP 27 cm H₂O, PEEP 10 cm H₂O, F_{IO_2} 0.50, and set ventilator rate 27 breaths/min. After the transition to CMV, ABG analysis revealed pH 7.37, P_{aCO_2} 66 mm Hg, P_{aO_2} 58 mm Hg. She was extubated after 8 days of CMV and remained in the hospital for an additional 12 days. She was discharged to home without the need for bronchodilators or oxygen.

Case 3. A 5-year-old boy with HbSS disease and a recent history of ACS was admitted after a 2-day history of cough, fever (40.6°C), and leg pain. On admission his white blood cell count was 32,800 cells/ μ L and hemoglobin was 6.5 g/dL. The white blood cell differential was 76% neutrophils, 6% bands, 2% lymphocytes, and 15% monocytes. He was tachypneic and in moderate distress, with blood oxygen saturation of 95% while breathing room air. The initial chest radiograph revealed right middle and lower lobe infiltrates and a right-sided effusion. During the first day of hospitalization he had frequent desaturations below 90%, despite supplemental oxygen. He was intubated and underwent exchange erythropheresis. Bronchoscopy was performed and large, yellow, rubbery casts were removed. He remained on F_{IO_2} of 1.0 after 24 hours of CMV, with an OI of 32 on maximum settings of PIP 33 cm H₂O, PEEP 10 cm H₂O, and ventilator rate 20 breaths/min. Subsequently, HFOV was initiated, and bronchoscopy was performed several hours later. Six hours after the initiation of HFOV the settings were F_{IO_2} 0.80, \bar{P}_{aw} 31 cm H₂O, amplitude 28 cm H₂O, and frequency 6 Hz (OI 35). After the first 12 hours of HFOV the OI had fallen to 21, F_{IO_2} had been decreased to 0.6, and \bar{P}_{aw} was 26 cm H₂O. Bronchoscopy was performed on 3 consecutive days. The OI decreased to 17 after 48 hours of HFOV. After 96 hours on HFOV the ventilation mode was converted to CMV and he was extubated 3 days later. He

was weaned from supplemental oxygen within 2 days and discharged to home 2 weeks later, without the need for any respiratory therapy.

Case 4. A 7-year-old girl with HbSS disease and a history of mild pain crises was admitted for an acute onset of respiratory distress. She was transferred from an outside hospital with fever (38.8°C), new-onset right-sided abdominal pain, and cough. Prior to transfer she received amoxicillin for presumed streptococcal pharyngitis. Her chest radiograph demonstrated an almost complete “white-out” of bilateral lung fields. She was immediately intubated and received an exchange transfusion upon PICU admission. Her initial ABG values were pH 7.38, P_{aCO_2} 42 mm Hg, and P_{aO_2} 90 mm Hg while receiving F_{IO_2} 1.0. Her admission hemoglobin was 6.2 g/dL and her white blood cell count was 35,000 cells/ μ L. She was initially placed on CMV, for 24 hours, but remained desaturated on F_{IO_2} 0.90, PIP 25 cm H₂O, PEEP 10 cm H₂O, and OI 30. Bronchoscopy successfully removed thick plugs from bilateral bronchial trees, and she was subsequently placed on HFOV. The initial OI on HFOV was 17. Forty-eight hours after intubation the patient had a chest tube placed for a moderate-sized pleural effusion. Sterile serous fluid was removed via the chest tube, and all cultures remained negative. She required dopamine 10 μ g/kg/min for the first 2 days of mechanical ventilation. She was supported for 5 days on HFOV, with a maximum OI of 17. A total of 5 bronchoscopies were performed. She was successfully converted back to CMV after 5 days of HFOV and was extubated 2 days later to noninvasive positive-pressure ventilation at PIP 12 cm H₂O and PEEP 4 cm H₂O. She was weaned to room air the following day and discharged to home on a prednisone taper.

Case 5. A 6-year-old boy with hemoglobin SO-Arab disease was admitted to a local hospital with sharp abdominal pain. Four months prior he had an episode of ACS that required a packed red blood cell transfusion and oxygen therapy. Initial hemoglobin and white blood cell values were 8.7 g/dL and 31,900 cells/ μ L, respectively. The differential was 65% neutrophils, 2% bands, 19% lymphocytes, and 14% monocytes. Initial chest radiograph was normal. Over the following 48 hours he developed bilateral lower-lobe pulmonary infiltrates and an increasing oxygen requirement. He was transferred to our institution in substantial respiratory distress; he was hypoxic on 4 L/min oxygen via nasal cannula and was unresponsive to bronchodilator therapy. He was intubated and the ventilator settings were PIP 40 cm H₂O, PEEP 10 cm H₂O, and F_{IO_2} 1.0. After 3 hours of CMV that required persistently high ventilator settings, his OI was 44 and the ventilator mode was converted to HFOV. HFOV was utilized for 55 hours, during which the initial OI was 62 and the final OI

was 13. The initial HFOV settings were \bar{P}_{aw} 28 cm H₂O, F_{IO_2} 1.0, amplitude 44 cm H₂O, and frequency 6 Hz, with corresponding ABG values of pH 7.28, P_{aCO_2} 63 mm Hg, P_{aO_2} 45 mm Hg. The chest radiograph showed dramatic improvement after 48 hours of HFOV. Bronchoscopy was performed on 3 consecutive days while the patient was on HFOV, and large mucus plugs were removed. He was weaned to CMV at PIP 28 cm H₂O, PEEP 10 cm H₂O, and F_{IO_2} 0.60. He was extubated 7 days later and discharged to home 4 days after extubation, without the need for bronchodilators or supplemental oxygen.

Case 6. A 12-year-old boy with HbSS disease and a history of pneumonia presented to his local clinic with a 4-day history of left upper-chest pain and a temperature of 38.0°C. His chest radiograph was reportedly negative. He developed an oxygen requirement and became diaphoretic. Upon transfer to our institution his admission hemoglobin was 5.6 g/dL and his white blood cell count was 51,000 cells/ μ L (69% neutrophils, 17% bands, 10% lymphocytes, 4% monocytes). His extremities were cool, capillary refill was 3 seconds, and urine output was decreased. He required 4 L of intravenous fluids and inotrope infusions (dopamine 10 μ g/kg/min, epinephrine 0.1 μ g/kg/min) to maintain adequate peripheral perfusion and urine output. The initial chest radiograph revealed multilobar infiltrates and bilateral pleural effusions. He complained of worsening leg and chest pain, and his respiratory status deteriorated, which required intubation. Initial CMV settings included PIP 21 cm H₂O, PEEP 5 cm H₂O, and F_{IO_2} 1.0. Over the first 24 hours he could not maintain adequate oxygen saturations above 90%, despite an F_{IO_2} of 1.0, so the ventilation mode was converted to HFOV. He underwent bronchoscopy while on HFOV, and a few small plugs were removed. After 6 hours on HFOV the F_{IO_2} had been decreased to 0.70 and the P_{aO_2}/F_{IO_2} ratio improved. After 48 hours his OI was 10 (F_{IO_2} 0.55 and \bar{P}_{aw} 25 cm H₂O) and the inotropic support was discontinued. After 84 hours of HFOV the ventilation mode was converted to CMV, with PIP 25 cm H₂O, PEEP 8 cm H₂O, and ventilator rate 12 breaths/min. He was extubated 2 days later and discharged to home 10 days after extubation, without any respiratory support.

Discussion

Severe ACS leading to hypoxemic respiratory failure may result from a combination of obstructive endobronchial secretions and progressive ARDS. In a given patient either of those entities may predominate and it may be difficult to distinguish the primary disturbance. This case series reports the first successful treatment of hypoxemic respiratory failure with HFOV and bronchoscopy. Oxygenation improved during HFOV, allowing for weaning

from potentially injurious oxygen supplementation and ventilator settings. HFOV was both safe and effective in this series of patients. All the patients were discharged to home without the need for supplemental oxygen or respiratory medications.

The 6 patients in our series presented with the typical clinical characteristics of ACS. Each patient developed acute respiratory failure and worsening hypoxia despite substantial CMV support. The exact pathophysiology of the severe hypoxia in each of our patients is not known but may have resulted from a combination of: severe acute chest pain with splinting and subsequent ventilation-perfusion mismatch related to atelectasis; severe airway obstruction; and/or primary acute parenchymal lung injury (infection and/or infarction).

Standard treatment for severe ACS must address the underlying clinical entities, which may include hypoxia, intravascular dehydration, vasoocclusion from red blood cell sickling, infection, and inspissated secretions that obstruct airways. Standard clinical management includes analgesia, intravenous fluid administration, broad-spectrum antibiotics, double-volume red blood cell exchange transfusions performed to a goal of $\leq 30\%$ HbS, inhaled respiratory medications (bronchodilators, N-acetylcysteine, and/or dornase alfa), and possibly intravenous steroids.^{2,10,25,26} Transfusion therapy has been the only conventional ACS therapy that has demonstrated impressive improvement in hypoxemia within a few hours to days.²⁵ Despite these supportive therapies, ACS can rapidly cause refractory hypoxemia and respiratory failure that requires mechanical ventilation.

Mechanical Ventilation

ACS with the development of obstructive mucus plugs and ARDS may place ACS patients at high risk for air trapping and barotrauma. This may be especially true of the more severely ill patients who require potentially injurious CMV ventilator settings and aggressive volume recruitment maneuvers. HFOV benefits pediatric patients with acute lung injury.²²⁻²⁴ However, HFOV may increase the risk of air trapping and barotrauma in patients with severe airway obstruction.^{23,24} In the acute phase of their illness ACS patients have an average forced expiratory volume in the first second (FEV_1) of 53% of predicted.⁹ Plastic bronchitis and/or other types of mucoid secretions may lead to bronchial obstruction that predisposes to the "ball-valve" effect of air trapping. Despite that clinical concern our case series indicates that HFOV can be successfully used with obstructive airways disease without an unacceptable degree of barotrauma. Each of our 6 patients met the criteria for ARDS as defined by the American-European ARDS Consensus Conference,²⁷ each was successfully managed with HFOV and bronchoscopy, and all

were discharged to home without supplemental oxygen or respiratory medications. None demonstrated hemodynamic instability or deteriorating respiratory status during HFOV. In fact, all 6 patients had substantial OI improvement during the course of HFOV (Table 2).

The initial OI increase during the transition from CMV to HFOV is somewhat artifactual. HFOV uses relatively high mean airway pressures to rapidly recruit lung volume without the need for elevated peak inspiratory pressure. This increases mean airway pressure before an oxygenation improvement is realized. Thus, the OI mathematical equation results in an initially increased number. No prior reports have described the use of HFOV for the management of ACS.

HFOV provides lung recruitment and may avoid end-inspiratory overdistention of relatively compliant nondependent lung regions.²³ HFOV may be particularly effective in ACS that causes ARDS, because it combines (1) improved alveolar recruitment, leading to better regional microvascular blood flow, and (2) smaller tidal volumes, allowing those lung areas with longer time constants to empty completely and to avoid regional air trapping.

Despite the theoretical concerns of using HFOV in diseases that predispose to air trapping and air leak syndromes, only one of the 6 patients developed subcutaneous emphysema and a small pneumothorax, which was easily treated with manipulation of an existing chest tube. The subcutaneous air was identified 24 hours after the initiation of HFOV and was observed for 2 days before a small pneumothorax was identified on chest radiograph. After evacuation of the pneumothorax it recurred 48 hours after conversion from HFOV to CMV. These cases suggest that HFOV and bronchoscopy should be strongly considered for patients with severe ACS and hypoxemic respiratory failure refractory to CMV.

Bronchoscopy

Perhaps our patients were successfully treated with HFOV because they underwent bronchoscopies to remove obstructive mucus plugs. In a retrospective review of 26 pediatric ACS patients undergoing diagnostic bronchoscopy, Moser et al reported plastic bronchitis to be present in 72% of cases.²¹ Few studies have commented on the therapeutic use of bronchoscopy for airway clearance in this patient population.^{2,9,19} Theoretically, removing the mucus plugs and clearing the multiple areas of airway obstruction will address the hypoxia and hypoxic pulmonary vasoconstriction. In the literature, bronchoscopy has generally been cited as a useful adjuvant to improve the appearance of the chest radiograph and to greatly improve infectious diagnosis in adults. Knight et al demonstrated that when bronchoscopy was performed in pediatric ACS patients for diagnostic purposes, there was marked clinical

HIGH-FREQUENCY OSCILLATORY VENTILATION FOR PEDIATRIC ACUTE CHEST SYNDROME

Table 2. Oxygenation During Mechanical Ventilation in 6 Pediatric Patients with Respiratory Failure From Acute Chest Syndrome

Ventilation Mode	P_{aO_2}/F_{IO_2} and (Oxygenation Index)					
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
CMV (pre-HFOV)	77 (27)	67 (35)	53 (32)	90 (23)	67 (44)	124 (8)
HFOV (initial settings)	66 (45)	127 (27)	80 (34)	137 (17)	45 (62)	105 (21)
HFOV (after 6 h)	95 (30)	135 (25)	68 (35)	223 (11)	68 (41)	270 (8)
HFOV (after 24 h)	138 (19)	163 (17)	118 (22)	162 (15)	69 (38)	140 (15)
HFOV (after 48 h)	124 (23)	149 (21)	140 (18)	193 (11)	176 (13)	244 (10)
CMV (24 h after HFOV)	249 (11)	158 (13)	207 (7)	360 (3)	200 (6)	362 (3)
Total Duration of Mechanical Ventilation (h)	318	391	192	180	234	154

F_{IO_2} = fraction of inspired oxygen

Oxygenation index = mean airway pressure $\times F_{IO_2} \times 100/P_{aO_2}$

CMV = conventional mechanical ventilation

HFOV = high-frequency oscillatory ventilation

improvement in a significant proportion of the patients.² In particular, N-acetylcysteine and deoxyribonuclease were beneficial in removing plastic-like secretions from the airways.^{2,18,19} However, bronchoscopy has never been shown to shorten the course of ACS nor change the mean duration of hospital stay.²¹

Factors that have been speculated to play a role in the formation of these casts include: impaired mucociliary clearance related to pain/splinting;²⁰ ischemia of the bronchial tree in vasoocclusive crisis, resulting in ciliary dysfunction;²⁰ increased lung blood volume during ACS;²⁸ and leakage of lymphatic fluid into the airway.^{19,20} The white, gray, yellow, or green casts have been described as being composed of organized aggregates of mucofibrinous substrate mixed with inflammatory cells.^{18,19,21} In our patients, bronchoscopy was generally completed in 10–15 min, resulted in the removal of several large mucus plugs, and led to improved OI and clearance of radiographic densities.

Conclusions

Based on the successful treatment of these 6 pediatric patients with severe ACS, we recommend the following treatment strategy: (1) Initiate standard supportive care, including double-volume erythropheresis, as soon as possible. (2) Use bronchoscopy as an adjuvant for secretion clearance in mechanically ventilated ACS patients. (3) Consider HFOV when CMV settings approach or exceed $PEEP \geq 10$ cm H_2O , $\bar{P}_{aw} \geq 15$ cm H_2O , $PIP \geq 32$ cm H_2O , or $F_{IO_2} \geq 0.60$, and/or $OI \geq 20$. Patients may be placed on HFOV without strong concern about impaired secretion clearance or air leak syndromes.

To minimize the risk of barotrauma and secondary lung injury it also seems reasonable to allow permissive hypercapnia.²³ With our patients we adjusted ventilator settings

to achieve arterial $pH \geq 7.25$ and $P_{aO_2} \geq 60$ mm Hg. Chest radiographs were used to monitor lung expansion. The mean airway pressure was adjusted to achieve a goal of 8–9 rib expansion of the lung fields on chest radiograph.

The etiology of ACS in a given patient is often unknown. Thus, clinicians should continue with the current standard of supportive care for ACS, including judicious fluid administration, exchange volume transfusion, broad-spectrum antibiotic coverage, and aggressive treatments to mobilize and remove mucus. However, when hypoxia becomes refractory to CMV, one should consider HFOV and bronchoscopy to improve oxygenation, to support lung expansion, and to improve airway patency while limiting barotrauma.

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