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CASE REPORT

High-frequency oscillatory ventilation in an infant with cystic fibrosis and bronchiolitis

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Summary Infants with cystic fibrosis (CF) may develop severe respiratory compromise related to viral lower respiratory tract infections due to impaired mucous clearance and plugging of small airways. Consequently air trapping may lead to lung hyperinflation, impaired gas exchange, and respiratory failure. We describe the case of an infant with newly diagnosed CF who developed severe hypercarbic respiratory failure in the setting of viral bronchiolitis successfully treated with high-frequency oscillatory ventilation (HFOV).

Introduction

Although not common, infants with cystic fibrosis (CF) may develop severe respiratory failure due to viral lower respiratory tract infections, such as bronchiolitis, which can carry a high mortality.[1,2] Both CF and bronchiolitis elicit physiological symptoms due to severe airflow obstruction in part due to mucus plugging of small airways. Moreover, in this setting once respiratory failure necessitates endotracheal intubation and mechanical ventilation, mucus clearance is further hindered. Though various means of chest percussion, postural drainage and mucolytics have been utilized to enhance airway clearance and reduce airway obstruction in CF-related bronchiectasis, their role in infants with CF and bronchiolitis is not established. While non-invasive high-frequency oscillatory ventilation (HFOV) has been used to enhance mucus clearance for patients with CF,[3] there are no reports of the successful use of HFOV in the setting of severe hypercapnic respiratory failure related to CF and

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bronchiolitis. Herein, we report on the successful effect of HFOV in the treatment of respiratory syncytial virus (RSV) bronchiolitis associated hypercapnic respiratory failure in an infant newly diagnosed with CF.

Case

A 5-month-old male was admitted to the hospital in August with cough and wheezing. Failure to grow was noted (length, ~40th %, weight, <3rd %). The parents recalled some possible malabsorption of formula. Physical exam was significant for diminished breath sounds with scattered wheezes throughout all lung fields. Respiratory rate was 45/min and noted to be labored. Oxygen saturation on room air was 85%. Continuous aerosolized albuterol by facemask and supplemental oxygen were administered. Within 24 h, the respiratory distress increased necessitating endotracheal intubation and mechanical ventilation (Siemens Servo 300C, Mode = pressure regulated volume control, inspired oxygen fraction (FiO_2) = 0.45, respiratory rate = 32/min, tidal volume delivered = 80 ml, peak pressure = 34 cmH_2O, positive end expiratory pressure (PEEP) = 5 cmH_2O) and mean airway pressure (MAP) = 8 cmH_2O. Thick, copious secretions were suctioned from the endotracheal tube. Ventilation was initially acceptable utilizing a hypercapnic strategy with an arterial blood gas (ABG) following equilibration during mechanical ventilation showing a pH of 7.18, $PaCO_2$ of 80 mmHg, and PaO_2 of 91 mmHg. RSV antigen was detected by enzyme immunoassay. A culture of airway secretions grew *Pseudomonas aeruginosa*, and *Enterobacter cloacae*. Sweat chloride was elevated at 88 and 87 meq/l, 163 and 146 mg, respectively. Subsequent testing revealed the presence of N1303K and 3659del C gene mutations for the cystic fibrosis transmembrane regulator (CFTR) protein confirming the diagnosis of CF. Aerosolized rHDNase was added to the regimen of intravenous cefepime, gentamicin, and aerosolized tobramycin.

Despite the addition of systemic corticosteroids, intravenous terbutaline, and helium–oxygen (70% helium, 30% oxygen) delivered through the ventilator, the patient failed to improve. By the fourth hospital day, respiratory acidosis worsened with an ABG showing a pH of 7.18, $PaCO_2$ >100 mmHg, and PaO_2 of 83 mmHg. Efforts to minimize dynamic hyperinflation by reducing inspiratory time and decreasing the respiratory rate to increase the inspiratory/expiratory ratio did not improve ventilation nor prevent the development of tension pneumothoraces requiring multiple chest tube placements.

The patient continued to have poor ventilation with repeated measurements of $PaCO_2$ >100 mmHg (Fig. 1). Mechanical ventilation was changed to HFOV (SensorMedics Oscillatory 3100A, Yorba Linda, CA) FiO_2 = 0.35, frequency = 7 Hz, inspiratory time % = 30, ΔP = 35 cmH_2O, MAP = 14 cmH_2O. Measurements of ventilation improved rapidly. As shown in Fig. 1, $PaCO_2$ declined significantly and the patient had no further recurrences of severe respiratory acidosis after the initiation of HFOV. In addition, the air leak, which had been ongoing during conventional mechanical ventilation (CMV), resolved. There was no significant hemodynamic compromise requiring intervention while on HFOV. After 4 days of HFOV, the patient was placed back on CMV for several days and successfully extubated. The patient remained in the hospital to optimize nutrition and was subsequently discharged home without the need for supplemental oxygen. On outpatient follow-up, the patient has had no further severe respiratory exacerbations and is thriving at this time.

Discussion

This case demonstrates the potential utility of HFOV in children with CF and severe hypercapnic respiratory failure due to viral bronchiolitis. We have shown an extended role of HFOV beyond the usual use in children with hypoxic respiratory failure. HFOV differs from CMV with regard to the mechanism of gas exchange between inspired gases and the alveoli. During HFOV, pressure oscillations up to 900/min are generated in the proximal airway which are associated with a constant, relatively high MAP and significantly smaller tidal volumes compared to CMV. Summation of gas exchange is likely to occur through a combination of various mechanisms including diffusion, Taylor dispersion, Pendelluft mixing, asymmetric velocity profiles, collateral ventilation, cardiogenic mixing and to a lesser extent, bulk transport.[4]

The current treatment of severe bronchiolitis is supportive care. Instillation of surfactant reduces mechanical ventilation by an average of 2.6 days, and ICU stay by 3.3 days, but immunoglobulin, glucocorticoids, and heliox have no significant effect.[5] Though HFOV has been reported in the management of refractory hypoxia in infants with bronchiolitis,[6] it is not generally recommended for respiratory failure in association with significant airflow obstruction because of the potential for frequency-dependent worsening of dynamic hyper-

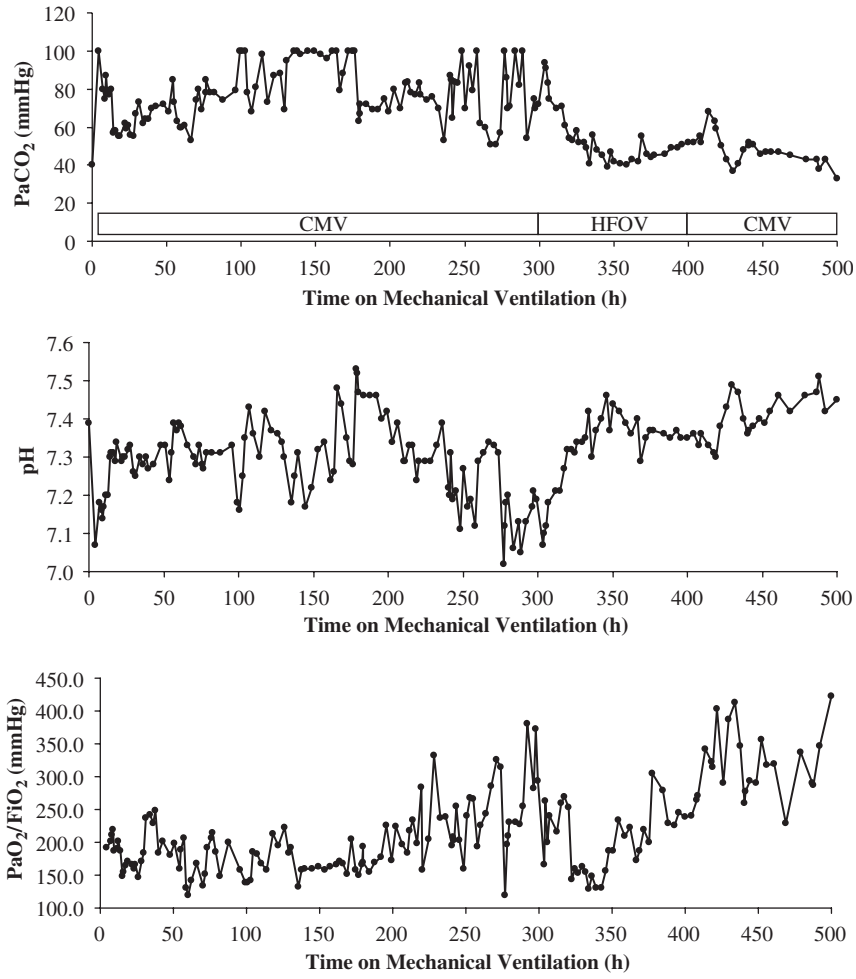

Figure 1 Panels indicate $PaCO_2$, pH, and PaO_2/FiO_2 during conventional mechanical ventilation (CMV) and high-frequency oscillatory ventilation (HFOV).

inflation.[7] Dynamic lung hyperinflation can increase the risk of barotrauma, dead space ventilation and hemodynamic compromise from diminished return of venous blood leading to low cardiac output. Despite these potential adverse effects, the successful use of high-frequency ventilation in respiratory failure with primarily obstructive pulmonary physiology has been reported.[8–11]

In this case we postulate that pharmacologic refractory random variations of mucus plugging and impaired airway clearance contributed to the observed stochastic severe elevations of $PaCO_2$ (>100 mmHg). We further postulated that HFOV, like other forms of airway oscillatory therapy[3] might improve mucus clearance and indirectly reduce dynamic hyperinflation thereby improving gas exchange. Our favorable result in this case is consistent with reports in older children with and without CF that have described the use of non-invasive high-frequency oral and chest wall oscillation to enhance mucus clearance in stable outpatients,[3,12] and in respiratory failure.[13]

A less commonly reported use of HFOV is the management of refractory hypoxia in infants with bronchiolitis.[6] Parallel with the recent evidence of improved outcomes in patients with acute respiratory distress syndrome (ARDS) who receive a low-tidal volume, "open lung" strategy during CMV,[14] there has been renewed interest in the use of HFOV in adults. Analogously, in our case an increased and constant MAP during HVOF compared to the MAP during CMV may have elicited an "open airway" strategy by opening airways closed by high surface tension. This latter mechanism may have reduced air trapping and lung hyperinflation and enhanced ventilation under these specific conditions. This latter hypothesis is in accordance with a recent report of a patient with status asthmaticus, where during HFOV, $PaCO_2$ was inversely related to increases in MAP.[8]

We recognize the possibility that the underlying airway inflammation, infection and mucus production may have been improving at the same time as the implementation of HFOV and thus improvements in pulmonary function were unrelated to the change in ventilator management. However, this seems unlikely given the magnitude and temporal correlation, as well as the durability of the improvement in ventilation after HFOV was initiated. In conclusion, our experience suggests promise for the use of HFOV in the management of severe hypercapnic respiratory failure refractory to CMV in infants with CF and viral bronchiolitis.

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