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Case Report

Use of Intrapulmonary Percussive Ventilation (IPV) in the Management of Pulmonary Complications of an Infant With Osteogenesis Imperfecta

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Summary. Osteogenesis imperfecta (OI) is a genetic disorder characterized by abnormal collagen formation and short stature. These patients present with frequent vertebral, rib, and long bone fractures. There are many respiratory complications associated with OI including pneumonia, the most common cause of mortality in the severe forms of the disease. We present a case of an infant with OI (type III/IV) and significant tracheobronchomalacia who had required multiple hospitalizations for recurrent atelectasis and respiratory failure in the setting of acute respiratory infections. External chest percussion and vibration were avoided because of the risk of rib fractures. intrapulmonary percussive ventilation (IPV) was initiated during an acute illness with good effect, and continued successfully after discharge from hospital. We conclude that IPV represents a safe and effective alternative to airway clearance in infants with OI. **Pediatr Pulmonol. 2009; 44:1151–1154.** © 2009 Wiley-Liss, Inc.

Key words: osteogenesis imperfecta; intrapulmonary percussive ventilation; airway clearance; atelectasis; tracheomalacia; bronchomalacia.

INTRODUCTION

Osteogenesis imperfecta (OI) is a genetic disorder characterized by altered synthesis of collagen type I, the primary component of the extracellular matrix of bone, skin, and connective tissues.[1] Most cases of OI are caused by a mutation in one of the two genes that encode the procollagen chains alpha1 and alpha2 (COL1A1 and COL1A2), on chromosome 17 and 7, respectively.[1,2] The CRTAP and LEPRE1 genes have also been implicated in moderate to severe/lethal forms of OI.[3] The pathological consequences of this abnormal collagen formation include increased bone fragility and overall impairment of connective tissue structure and function. Patients with moderate or severe forms of OI can present early in life with a variety of respiratory-related problems including rib fractures, chest wall abnormalities, upper airway obstruction, tracheomalacia, bronchomalacia, and recurrent atelectasis.[2,4–6] The latter abnormalities can be associated with chronic respiratory failure[4,7,8] probably related to hypercapnic hypoventilation and/or non homogeneous regional ventilation. In addition, respiratory infections are the leading cause of death in the severe forms of OI at all ages.[9] This may be related to inadequate airway clearance resulting from collagen-related structural defects in the airways and chest walls of these patients.[1,10,11] Traditional means of augmenting airway clearance such as chest percussion and vibration are seldom possible due to the risk of fractures in these children. Alternative means of achieving adequate airway clearance thus are clearly important in this group of patients.

We present the case of an infant with a severe form of OI (type III/IV), documented tracheobronchomalacia and recurrent atelectasis associated with respiratory infec-

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tions. The patient was successfully treated with intrapulmonary percussive ventilation (IPV) during an acute illness. Prophylactic use of IPV was continued subsequent to hospital discharge, with good effect. To our knowledge, this is the first report using this technique of airway clearance in a patient with the severe form of OI in this age group.

CASE REPORT

A 14-month-old male infant was born at 34 weeks gestation to a 37 year-old, gravida 3, para 2 female. Delivery was via emergency C-section because of maternal pre-eclampsia. Prenatal evaluation showed shortened limbs and bilateral femoral and ulnar fractures, raising concerns for OI. Postnatally, he suffered skeletal fractures of both femurs, the right humerus, multiple ribs, the left hand, and the right skull. A diagnosis of OI was suspected clinically and confirmed by skin biopsy and analysis of fibroblast collagen synthesis. Immediately after delivery, the infant was noted to have a weak cry, cyanosis, and poor respiratory effort requiring endotracheal intubation and mechanical ventilation. Apgar's scores were 3 and 8 at 1 and 5 min, respectively. He remained intubated for the first month of life but continued to experience significant respiratory distress after extubation associated with marked stridor. Examination by flexible bronchoscopy demonstrated moderate laryngomalacia, and diffuse tracheobronchomalacia. Vocal cord mobility was normal and there was no evidence of subglottic stenosis. Nasal continuous positive airway pressure (CPAP) of 8 cmH_2O was used via a nasal prong interface. Despite improvement in his respiratory status, he continued to require high amounts of supplemental oxygen and experienced recurrent episodes of lung atelectasis (Fig. 1A). A laparoscopic fundoplication and feeding gastrostomy were performed because of the presence of gastroesophageal reflux, poor feeding, and concerns for aspiration. After 5 months of hospitalization in the Neonatal intensive care unit, he was discharged home.

Two weeks later he was re-admitted with severe respiratory distress. Initially he was supported by continuous non-invasive ventilation but subsequently he required airway intubation and mechanical ventilation for respiratory failure. Rapid viral detection studies showed the presence of Human Metapneumovirus in respiratory secretions. Over the following weeks, his secretions continued to be copious and chest radiographs demonstrated persistent atelectasis (Fig. 1B). He was treated with antibiotic therapy, frequent nebulized bronchodilator aerosols, and systemic corticosteroids for associated reactive airway disease. Therapy with inhaled human recombinant DNase (dornase alfa) was commenced with little change in clinical status. No chest percussion or vibration was attempted because of the infant's underlying disorder. He slowly recovered, and at 7 months of age he was discharged home. His therapies included 1 lpm of supplemental oxygen by nasal cannula, daily use of inhaled corticosteroids, frequent bronchodilator therapy, and nasal CPAP at night.

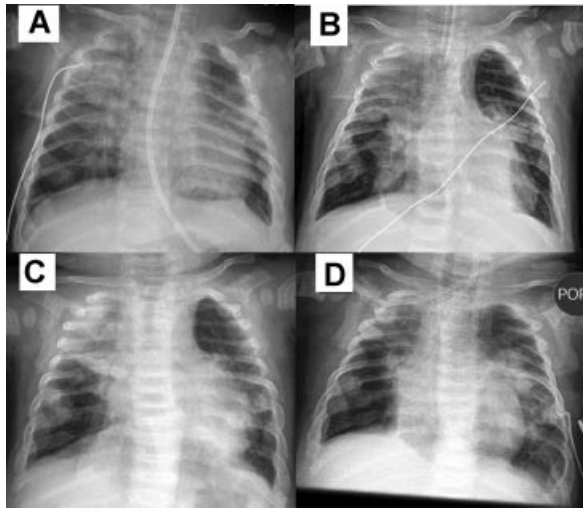

Fig. 1. Chest radiographs demonstrating multiple rib fractures and diffuse areas of wandering atelectasis. These films were taken at 3 months (A), 6 months (B), and 7 months (C) of age. Aeration of the right upper and left lower lobes improved 48 hr after starting IPV therapy (D).

Three weeks after discharge he was re-admitted into the intensive care unit with acute respiratory distress, an increased supplemental oxygen requirement and new opacification of his right upper and left lower lobes (Fig. 1C). In light of his respiratory status and history of recurrent atelectasis, IPV was initiated every 2 hr to improve his airway clearance. The IPV treatments lasted 15–20 min and the parameters utilized were 1:2.5 i/e ratio, frequencies between 180–300 per minute and the peak pressure was initially set at 20 cmH_2O. He tolerated this technique well, using a small cushioned facial mask and a Percussionator IPV-1 device (Percussionaire Corp., Sandpoint, ID; Fig. 2A,B). Careful evaluation of his chest wall, face, and skull did not reveal any new fractures after starting this therapy. Within 2 days of initiating IPV, the areas of atelectasis improved (Fig. 1D) and his supplemental oxygen requirement decreased. Three days later he was discharged home breathing room air without need for nocturnal CPAP. After discharge IPV was continued four times per day and then its frequency decreased to two times daily to provide a baseline regimen for airway clearance. He has also received additional IPV treatments as needed for symptoms and during acute respiratory illnesses. His ambulatory follow-up has demonstrated adequate tolerance to this therapy without the presence of new fractures. In the 6 months since the initiation of IPV, there have been no subsequent hospitalizations for respiratory distress, pneumonia, or atelectasis.

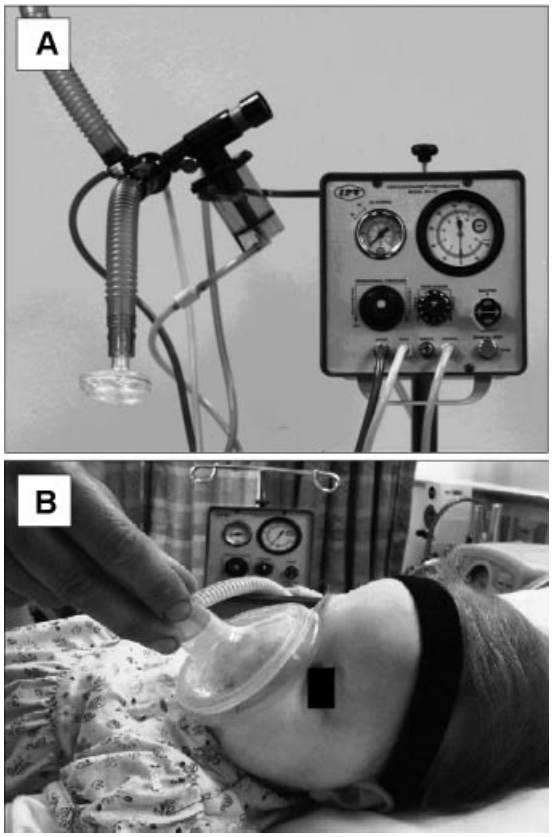

Fig. 2. Intrapulmonary percussive ventilation device (Percussionator IPV-1C, Percussionaire Corp.) (A). Infant undergoing intrapulmonary percussive ventilation through a face mask in a lying position (B).

DISCUSSION

Our patient was diagnosed with a severe type of OI (III/IV). He suffered multiple skeletal fractures and had significant tracheobronchomalacia and recurrent atelectasis (Fig. 1). During his first 7 months of life he required several prolonged admissions to the intensive care unit because of respiratory failure associated with lung collapse and respiratory infections. These probably resulted from, or at least were exacerbated by his inability to clear secretions appropriately. The use of IPV via a small cushioned facial mask (Fig. 2A,B) resulted in a dramatic improvement in his respiratory status without causing skeletal fractures. Within a few days of initiation of this therapy the atelectasis had improved significantly (Fig. 1D) and his supplemental oxygen requirement resolved. IPV helped in the management of his acute respiratory illness and its daily use has helped to prevent further hospital admissions from atelectasis and respiratory failure.

There are many potential respiratory complications in patients with the severe forms of OI. Multiple rib fractures, kyphoscoliosis and pectus deformities can cause anomalous chest wall configurations leading to abnormal breathing mechanics.[2,6,12] Central respiratory function can be affected by brainstem compression due to basilar impression.[8] Significant extrathoracic airway obstruction can occur secondary to laryngomalacia or glottic narrowing.[4,5] These disorders can be severe enough to cause impairment of gas exchange and chronic respiratory failure. Although non-invasive ventilation techniques to deliver CPAP or Bi-level positive airway pressure (BLPAP) have been described in patients with OI,[7] patients with more severe disease sometimes need the placement of artificial airways (i.e., tracheostomy) to ensure adequate ventilation and oxygenation.[4,8]

There are also significant abnormalities seen in the lower airways of patients with OI. Altered synthesis of collagen type I is the characteristic pathological feature of all types of OI.[1] This type of collagen is a critical determinant of tensile strength in various pulmonary structures, including airway walls and interstitial tissue.[11,13] The clinical manifestations of this molecular defect in the lung include pulmonary hypoplasia,[10] tracheobronchomalacia, atelectasis, and recurrent pneumonia.[2,4,9] The fact that pneumonia and other respiratory infections are by far the most common cause of death in the severe forms of OI[9] emphasizes how the disease-related structural defects of the respiratory system impair airway clearance.

Altered airway clearance poses several challenges for patients with OI. Multiple rib fractures and abnormal chest wall configuration can affect the ability of these patients to generate precough lung volumes high enough to store adequate kinetic energy in the form of elastic recoil.[6,12,14] In those patients with tracheobronchomalacia, increased airway compliance will cause considerable dynamic compression of central airways during the expulsive phase of cough.[14–16] These phenomena can prevent the production of the high expiratory flow rates necessary for appropriate clearing of secretions, thereby, increasing the risk of lung infections.[14,15] These physiological abnormalities accompanying the severe forms of OI can at least partially explain the predisposition of these patients to develop persistent atelectasis and recurrent pneumonia.

Several techniques aimed at clearing airway secretions, particularly during acute infections, have been developed for patients with abnormal mechanisms of mucociliary clearance.[14,17] Many of these techniques are designed to enhance mucus mobilization,[14,17] while others are aimed at mucus extraction. While manual chest percussion and vibration with postural drainage or high-frequency chest wall oscillation devices (i.e., The Vest Airway Clearance System) are accepted techniques for mucus mobilization, the risk of causing rib fractures makes the administration of these therapies problematic.[14,17,18] IPV aids mucus mobilization by delivering high flow, low-volume ''mini-

bursts'' of positive pressure to the airways at frequencies ranging from 100 to 300 cycles/min.[14,17,18] These rapid frequencies create an internal percussive effect that is more likely to break up mucus cohesion and adhesion and thus mobilize secretions.[19] The intrapulmonary percussions maybe superimposed on the patient's spontaneous ventilation as a dynamic CPAP and can provide a baseline distending pressure that increases airway caliber.[14,18,19] The air delivered travels beyond the secretions and then moves them towards more central airways following the expiratory pressure.[14,18]

IPV also allows the delivery of aerosolized medications,[14,18] but given its high cost and the large variability of its intrapulmonary deposition, the device is not recommended as a first choice for inhaled drug therapy.[20] As a technique of airway clearance, IPV has been shown to be effective and well tolerated when used for the treatment of persistent atelectasis in adults[18] and in children.[21–23] In our patient, we believe that the positive end-expiratory pressure together with the vibratory and percussive effects provided by the device were critical factors to enhance airway clearance and improve his persistent atelectasis.

In summary, we present the first description of the use of IPV for the prevention and treatment of recurrent atelectasis in an infant with a severe form of OI (type III/IV). We conclude that IPV represents a safe and effective alternative for the management of airway secretions in OI. This strategy can potentially help in the prevention of the serious respiratory complications associated with this disease.

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