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Noninvasive Ventilatory Strategies in the Management of a Newborn Infant and Three Children With Congenital Central Hypoventilation Syndrome

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Summary. Four children with congenital central hypoventilation syndrome (CCHS) treated with noninvasive techniques of ventilation are presented. Two infants (one in the newborn period) were treated with nasal mask bilevel positive airway pressure (BiPAP), and then both were transitioned to negative pressure chamber ventilation at several years of age because of possible midface hypoplasia. Tracheostomies were not performed. Two older children were transitioned from mechanical ventilation via tracheostomy to nasal mask BiPAP, and then in one case to negative pressure chamber ventilation, and in the other to phrenic nerve pacing. Their tracheostomies were removed. **Pediatr Pulmonol. 2003; 36:544–548.** © 2003 Wiley-Liss, Inc.

Key words: congenital central hypoventilation syndrome; noninvasive ventilation; BiPAP; negative pressure ventilation; midface hypoplasia; Moyamoya disease.

INTRODUCTION

Mechanical ventilatory assistance is necessary for survival in infants and children with congenital central hypoventilation syndrome (CCHS). However, it may be necessary to alter the mode of ventilation according to age, psychosocial reasons, complications of therapy, progression of disease, and emergence of new modes of ventilation.

We present our experience of noninvasive strategies in the respiratory management of a series of four children with CCHS. Two were managed with these techniques for 6 and 7 years, respectively, with one of these from the newborn period. Two older children, aged 11 and 16 years, were transitioned to noninvasive ventilation techniques after initially receiving mechanical ventilation via tracheostomy.

CASE ONE

This 16-year-old girl hypoventilated within hours of birth and has required respiratory support during sleep her entire life and for the past year while awake. A polysomnographic study at age 2 years confirmed inadequate spontaneous ventilation during delta sleep, when pulse oximetry (SpO_2) decreased to 53% and transcutaneous partial pressure of carbon dioxide ($TcpCO_2$) increased to 76 mmHg. Subsequent studies revealed a lack of ventilatory response to hypoxemia and hypercarbia during sleep. In the newborn period and for 15 years, she ventilated adequately while awake, but during respiratory infections in the first 2 years of life, daytime ventilation and oxygen therapy were required.

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She also has other minor autonomic dysfunctions, including peripheral cyanosis in cold weather, dry eyes and mouth, and constipation.

A tracheostomy was performed, and at the age of 2 months and at 11 months she was discharged home with nocturnal mechanical ventilation. Trials of nasal mask bilevel positive airway pressure (BiPAP) (Respironics, Inc., Pittsburgh, PA) were unsuccessful at ages 5 and 6 years, mainly because of a lack of tolerance for the mask.

At age 9 years, her parents requested noninvasive ventilation and removal of the tracheostomy in a bid to reduce the number of lower respiratory infections, which had resulted in 24 hospital admissions. A trial of negative pressure ventilation by chest cuirass was undertaken but was abandoned when SpO_2 could not be consistently maintained above 93%.

At age 11 years, a nasal mask was better tolerated, and nasal mask BiPAP was successfully applied. The tracheostomy was downsized (to permit free gas flow around it from pharynx to lungs) and corked. The tracheostomy was removed 1 month later. No further lower respiratory tract

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infections requiring hospitalization have occurred. The use of nasal mask BiPAP initially reduced and eventually abolished the need for awake carers at her bedside. A residual tracheo-cutaneous fistula required surgical closure. During upper respiratory tract infections, nocturnal ventilation by mask BiPAP is still adequate, and she has not required hospital admission or tracheal intubation until onset of daytime hypoventilation.

At age 15 years, awake hypoventilation was recognized by daytime somnolence, deteriorating school performance, and hypoxemia (SpO_2 68–76%). Pulmonary hypertension was suspected on the basis of tricuspid incompetence (jet 2.9 m/sec) detected by echocardiography. Implantation of bilateral phrenic nerve pacing (Atrostim Jukka, Atrotech, Tampere, Finland) was performed for use during the daytime, but she continues to receive nasal mask BiPAP when asleep. Echocardiographic evidence of pulmonary hypertension subsequently resolved over several months. However, a 24-hr ECG study revealed 12 episodes of sinus bradycardia and sinus pauses lasting up to 4.6 sec.

Subsequently, she presented with facial nerve palsy, focal fits, and mental deterioration, which were attributed to extensive Moyamoya disease diagnosed by cerebral angiography. Multiple burr holes were performed in a bid to neovascularize the cerebri, but the disease progressed to fatal cerebral infarction. No previous association between CCHS and Moyamya disease has been reported.

CASE TWO

This 11-year-old girl hypoventilated with intermittent periods of apnea at 6 hr of age after normal delivery. A cranial CT and MRI scan revealed no abnormalities. A polysomnographic study at age 1 month revealed long episodes of apnea with no response to hypoxemia and hypercarbia during both tonic REM and non-REM sleep. SpO_2 decreased to 48%, and $TpcCO_2$ increased to 72 mmHg. Repeated studies at 1 and 7 years of age revealed persistent nocturnal hypoventilation. Respiration was adequate while awake. Associated ophthalmic problems were unilateral ptosis, a divergent squint, and a Marcus-Gunn jaw-winking phenomenon. Constipation led to a rectal biopsy, which excluded Hirschsprung's disease.

A tracheostomy was performed, and she was discharged home at 16 months of age with volume-cycled mechanical ventilation. Carers (trained lay-persons) were provided 6 nights per week. When upset, she was able to breath-hold, which occasionally led to loss of consciousness and onset of hypoxic-induced grand mal convulsions. Initially, these episodes occurred 3–4 times per year, but became infrequent with advancing age and have not occurred since age 6 years. On such occasions, bag-to-tracheostomy ventilation promptly relieved hypoxemia and convulsions. An electroencephalogram did not reveal any abnormality, and anticonvulsants were not used.

At age 9 years she wanted her tracheostomy removed. The tube was downsized from 5.5 to 4.0 mm and corked. Her ventilation was changed to a pressure plateau ventilation mode[1] as an interim step to conversion to nasal mask BiPAP (Model S/T-D 30, Respironics, Inc.), which was adopted routinely after several months of training and intermittent use. BiPAP pressures were 24/4 cm H_2O, with 12 breaths per minute in the timed/spontaneous mode.

At age 10 years, a successful trial of negative pressure chamber ventilation (Porta-lung and NEV-100 Negative Pressure Ventilator, Respironics, Inc.) was conducted with the tracheostomy corked. Approximately 1 night in 10 while in supine position, mild upper airway obstruction caused SpO_2 to decline to approximately 90%. These were promptly relieved when her body position was shifted by her carer from supine to lateral, or when she was aroused from sleep. At age 11 years, the tracheostomy was removed, and upper airway obstruction has not been problematic. On recovery from general anesthesia for repair of the tracheostomal fistula, she required Naloxone to reverse fentanyl-induced (0.5 mcg/kg) hypoventilation. A subsequent polysomnographic study performed with ventilator settings at −16/0 cm H_2O at 16 breaths per minute revealed normal sleep architecture, an arousal index of 11.6/hr (none due to respiratory events), a minimum SpO_2 of 98%, low $TcpCO_2$, and occasional brief (2–3 breaths) audible snores, but with no discontinuation of nasal air flow the entire night uninterrupted in supine or semisupine position. Eyelid surgery and strabismus correction were performed.

CASE THREE

This 6-year-old boy presented in the newborn period with hypoventilation and episodes of apnea. Although Apgar scores were recorded as 9 at 1 min and 10 at 5 min, some ventilation by mask had been required in the immediate perinatal period. Several hours after birth, endotracheal intubation and mechanical ventilation were required for hypoventilation. He was extubated at 13 days of age, but reintubation and ventilation were again required at 15 days of age. A CT and MRI study of the brain did not reveal any abnormality. A diagnosis of CCHS was made by a polysomnographic study which revealed hypoventilation during REM sleep. Arousal did not occur when SpO_2 declined to $<50\%$. When hypoxemia was prevented with oxygen administration, no response was provoked, even when $TcpO_2$ reached 81 mmHg. Adequate spontaneous ventilation was present while awake. Hirschsprung's disease was diagnosed by colonic biopsy after bowel obstruction occurred.

The infant's parents were adamant that tracheostomy not be performed. A trial of BiPAP (Respironics, Inc.)

administered by nasal mask was attempted at 6 weeks of age. This was tolerated immediately, and yielded a $PaCO_2$ of 40–50 mmHg. A training program to enable parental care at home with the aid of carers was instituted, and the infant was discharged at age 4 months.

At age $2\frac{1}{2}$ years, midfacial hypoplasia was suspected because of apparent mandibular protrusion. Clinical examination confirmed that the maxillary teeth lay several millimeters behind the lower incisors (class 3 dental malocclusion). A trial of negative pressure chamber ventilation (Porta-lung and NEV-100 Negative Pressure Ventilator, Respironics, Inc.) proved successful, and this technique was adopted, although nasal mask Sullivan VPAP (variable positive airway pressure, ResMed, Sydney, Australia) is still utilized when away from home or travelling in aircraft overnight.

CASE FOUR

This 7-year-old boy presented at age 5 weeks with episodes of cyanosis. A diagnosis of CCHS was made with a polysomnographic study at 11 weeks of age. At the onset of REM sleep, $TcpCO_2$ increased to reach typical plateaus of 70 mmHg in quiet sleep, while SpO_2 decreased to 64%. His condition was judged as ''mild,'' and he was discharged home with nocturnal oxygen therapy. Other investigations included a brain MRI study, an EEG, urine and plasma metabolic screening, and an echocardiogram, which were all normal. A Holter monitor study revealed a predominant sinus tachycardia and frequent ventricular extrasystoles. He presented again at age 9 months with mild dilatation of the right ventricle, trivial tricuspid incompetence, and pulmonary artery pressure estimated at least 55 mmHg by echocardiography.

His parents did not want a tracheostomy to be performed. He was treated with nasal mask BiPAP, to which he adapted over a period of 6 weeks. Subsequently, the pulmonary hypertension abated over a period of 4 weeks.

At age 3 years, concern arose over the pressure-related effects of nasal mask BiPAP. A lateral cephalogram demonstrated a class 3 dental malocclusion and flattening of the premaxilla, similar to the characteristics of midface hypoplasia. Negative pressure chamber ventilation was attempted and succeeded after an adaptation period of several weeks. Presently, he employs nasal mask BiPAP while falling asleep, and then switches to negative pressure chamber ventilation (Porta-lung and NEV-100 Negative Pressure Ventilator, Respironics, Inc.). Airway obstruction has not occurred.

DISCUSSION

A major problem in the respiratory management of CCHS is the choice of assisted ventilation, expected to be life-long due to the genetic basis of the disease.[2] Among the factors which determine the choice of technique are efficacy, practicality, psychosocial acceptance, complications, and cost. Techniques include intermittent positive pressure ventilation via tracheostomy, phrenic nerve pacing, noninvasive positive pressure ventilation (NPPV), and negative pressure ventilation by body chamber or cuirass.

Although mechanical ventilation is facilitated via tracheostomy and is regarded as the standard means of respiratory support for CCHS, it is not ideal. Tracheostomy in children per se has mortality and morbidity,[3] and is associated with impaired speech and language development[4] and with frequent colonization and infection of the lower airways.[5]

We have observed that tracheostomy is not mandatory, and that NPPV techniques are possible from birth or young infancy, and that transition from invasive techniques to NPPV is possible during childhood.

The impetus to use noninvasive techniques for the respiratory management of CCHS is multifactorial. In our series, this included psychosocial reasons, in particular avoidance or removal of a tracheostomy in late childhood and early adolescence. In addition, the availability of NPPV machines, which provide flow-triggered breaths with automatic breath-by-breath compensation for air leaks, and the advent of soft self-molding or cushioned nasal masks, all represent a practical and reliable alternative to invasive mechanical ventilation. Mask NPPV equipment is generally more transportable than a mechanical ventilator, and may be used easily away from home or during a car journey when the child falls asleep. Lastly, the possible requirement for less attendant care with noninvasive techniques is financially attractive. All these attributes of NPPV generally outweigh the disadvantages and complications such as aerophagia and facial pressure sores, which in any case can be easily avoided.

All children in our series were managed for varying periods with nasal mask BiPAP or VPAP. The first successful uses of nasal mask ventilation for CCHS were reported in 1987 in a 6-year-old child,[6] and in 1990 in a 9-year-old child who had previously received mechanical ventilation.[7] The youngest age at which nasal mask BiPAP has been applied for CCHS is 9 months.[8] However, no previous applications of nasal mask BiPAP for CCHS from the newborn period have been described.

Despite its advantages, long-term nasal mask BiPAP for young infants and children in the home setting is neither trouble-free nor wholly practical. An attendant is usually required to ensure that a nasal mask remains in place without significant air leakage for the whole of the sleep cycle. Importantly, prolonged use of nasal mask ventilation may lead to pressure-induced maxillary distortion. During long-term BiPAP, the maxilla may fail to advance with growth in relation to the mandible (midfacial hypoplasia), such that the lower jaw protrudes to create pseudoprognathism.[9] To confidently make this diagnosis,

accurate serial measurements of facial bone structure are required.

Several cases of pseudoprognathism or midface hypoplasia have already been reported. Pseudoprognathism was identified in a 17-year-old who had used nasal mask BiPAP for $3\frac{1}{2}$ years, and in an 11-year-old who had used nasal mask BiPAP for 3 years. In the former case, the diagnosis was made by comparative photography.[9] Midface hypoplasia was recognized in a 7-year-old who had received nasal mask BiPAP since age 9 months for CCHS.[8] This was rectified by application of a Delaire mask (a standard orthodontic device) which allowed minimization of the pressure on the face.[10] Midface hypoplasia was reported in a 15-year-old after 10 years of nasal mask CPAP for obstructive sleep apnea.[11]

Avoidance of positive pressure ventilation and consequent pulmonary barotrauma is an important goal in long-term ventilation. Three of the children in our series utilized negative pressure chamber ventilation. Although this technique simulates normal ventilation and is the least invasive, it may be neither wholly practical nor psychosocially acceptable. The apparatus is not easily transported and costs approximately AUD$50,000. Negative pressure chamber ventilation without tracheostomy may be used soon after birth, but supplementation with nasal mask CPAP or nasopharyngeal airway insertion may be needed to relieve upper airway obstruction, while endotracheal intubation and ventilation may be needed during respiratory tract infections.[12] Negative pressure chamber ventilation may cause upper airway obstruction in CCHS, because passive inspiration causes phasic epiglottic collapse.[13] Indeed, in seven other children treated with this technique, three required short periods of nasal mask CPAP or nasopharyngeal airway insertion to relieve upper airway obstruction, while four required endotracheal intubation and positive pressure ventilation during respiratory tract infection.[12] One of these children developed Moyama disease.

For the child who has a 24-hr requirement for respiratory support, phrenic nerve pacing is the only practical alternative, at least during wakefulness. This technique has the disadvantages of being invasive and expensive, at around AUD$100,000 for equipment and with additional costs for surgery, anesthesia, and hospitalization. In addition, it is expected that the components must be replaced at intervals of approximately 7–10 years. However, for such children, the possibility exists for 24-hr pacing and removal of tracheostomy. Although we elected to restrict phrenic nerve pacing to daytime in the child with 24-hr hypoventilation, the technique may be used day and night.[14]

Cost should be considered when selecting a life-long respiratory therapy. The largest portion is the provision of nighttime attendants. In our environment, the annual cost of providing a specifically trained lay care attendant 7 nights per week is AUD$102,000. Such attendants are probably necessary for a child who is receiving mechanical ventilation via tracheostomy, but not for an older child managed with nasal mask BiPAP or negative pressure chamber ventilation. Capital and consumable costs (AUD$) considered together are cheapest with the Porta-lung. The present capital cost for BiPAP (Respironics, Inc.) is approximately $24,000, compared with $46,000 for a Porta-lung and $22,000 for our current preferred home mechanical ventilator (Newport HT50). Approximate consumable costs for mechanical ventilation are $53,000, $26,000 for BiPAP, and $3,500 for Porta-lung. Added to these costs are required contributions to the salaries of our management team, consisting of intensive care physicians, nurse supervisors and trainers, technologists, and administrators.

The transition from mechanical ventilation via tracheostomy to nasal mask BiPAP may be difficult. Transition is not usually successful if the child is less than age 7 years,[15] which we observed in one of our cases at ages 5 and 6 years. Direct transition to negative pressure chamber or cuirass ventilation may be easier.

Ongoing monitoring is important once the patient is established at home with noninvasive respiratory assistance. Routine pulse oximetry is essential, and periodic checks of ventilation should be undertaken by monitoring end-tidal or transcutaneous carbon dioxide levels. End-tidal carbon dioxide monitoring is not practical during mask BiPAP. ECG Holter monitoring should be performed every 6–12 months to check for emergence of bradyarrhythmias,[16] which may require cardiac pacing. Echocardiography should be performed similarly to check for evidence of pulmonary hypertension, although the avoidance of chronic hypoxemia should prevent it.

We suggest that management of a newborn diagnosed with CCHS could initially be with nasal mask BiPAP upon cessation of mechanical ventilation via endotracheal tube in the first few weeks of life. Tracheostomy can be avoided. However, preparations should be made to trial negative pressure chamber or cuirass ventilation as soon as practicable, to avoid the problems of midface hypoplasia and pseudoprognathism associated with prolonged nasal mask BiPAP. If upper airway obstruction occurs during negative pressure ventilation, limited mask CPAP may be beneficial. If hypoventilation is present during wakefulness, phrenic nerve pacing is the only practical alternative from the time the patient becomes ambulant, but airway obstruction during sleep with this technique may limit its usefulness.

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