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Congenital central hypoventilation syndrome

A report of successful experience with bilateral diaphragmatic pacing

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SUMMARY Bilateral diaphragmatic pacing was successfully performed in an 18-month-old child with congenital central hypoventilation syndrome (Ondine's curse) as an alternative to long-term mechanical ventilation. Subsequent complications were related more to cor pulmonale and tracheostomy care than to the pacing itself.

Congenital central hypoventilation syndrome (CCHS), often referred to as 'Ondine's curse', is a rare disorder of ventilatory control, characterised by hypoventilation during sleep. Patients with this disorder require long-term mechanical ventilation, and most eventually develop fatal cor pulmonale. Few paediatric cases have been reported. Hunt *et al.*¹ reported the successful treatment of 3 infants with this condition, using radiofrequency diaphragmatic pacing. This report describes another successful experience using bilateral diaphragmatic pacing in the treatment of an 18-month-old child with CCHS.

Case history

A term boy, weighing 2992 g, was born after an uncomplicated pregnancy, labour, and delivery. Apgar scores were 7 and 8 at one and five minutes. During the first 8 hours of life, the infant experienced apnoeic episodes while sleeping. Serum electrolytes, glucose, calcium, and magnesium determinations were normal. Cerebrospinal fluid examination was normal. Chest x-rays showed no cardiomegaly or pulmonary disease. Skull x-rays, cranial com-

puterised tomography, and electroencephalograms were normal. The apnoeic episodes were initially treated with nasal continuous distending airways pressure and, later, with intravenous aminophylline. Neither treatment was successful.

On the third day of life, the infant was intubated and intermittent mandatory ventilation was administered during sleep. During the next 2 months, he received therapeutic trials with atropine, caffeine citrate, progesterone, thyroxine, oral doxapram, and phenobarbitone. None of these drugs was successful in preventing hypoventilation during sleep. A tracheostomy was performed at 2 months of age. Bronchoscopy and fluoroscopy of the trachea were normal. A carbon dioxide ventilatory response during sleep showed no increase in minute ventilation, despite increases in alveolar CO₂ to 60-80 mmHg. Ventilation was normal when awake.

At 6 months of age, he was sent home with a volume preset ventilator for respiratory assistance during sleep. However, during the next 2 months, the child and his family experienced many mechanical problems with the ventilator, pulmonary toilet, and recurrent pulmonary infections. Eventually, parental stress necessitated readmission. At that time, the patient's chest x-ray showed mild cardiomegaly. His electrocardiogram showed right ventricular hypertrophy. Both of these findings were consistent with the diagnosis of early cor pulmonale. Cor pulmonale was treated with chronic diuretics and the administration of 30% oxygen during spontaneous wakeful breathing and during mechanical ventilation when asleep.

At 18 months of age, bilateral phrenic nerve

electrodes and radio receivers were surgically implanted. The electrodes were placed on the lower thoracic portion of each phrenic nerve. The radio receivers were implanted subcutaneously in the anterolateral abdominal wall. The receiver, electrode cuff, and antennae were the same radiofrequency pacemaker system used in previous reports (Avery Laboratories, Farmingdale, NY).¹⁻² The external transmitter (Model S242, Avery Laboratories) differs from previous systems in that the threshold and amplitude controls are separate. There are 4 modes of operation permitting unilateral, alternate side, or simultaneous bilateral pacing. The respiratory rates ranged from 9–50 breaths/minute, and the inspiratory/expiratory ratio is a constant 1:2. Pacing was initiated on the 10th postoperative day. Simultaneous bilateral pacing during sleep was begun at a respiratory rate of 20 breaths/minute. The amplitude of the electrical stimulus was adjusted until tidal volumes of 10–12 ml/kg and end tidal CO₂ values measured between 35 and 40 mmHg. End tidal CO₂ measurements were made with an infrared CO₂ analyser (Cavitrone Model PM2ONR). Tidal volumes and minute volumes were measured with a Godart pneumotachograph (type 17212).

The patient was discharged 3 weeks after surgery. He was readmitted one week later because of problems with pulmonary toilet. An air conditioner and electrostatic air purifier were installed in the infant's home and subsequent mechanical airway problems were slight. However, he was admitted to hospital on several occasions for intercurrent pulmonary infections.

The child is now 25 months old. A Denver Developmental Screening Test performed at 22 months of age was normal except for speech and failure to feed with a spoon. Because of refusal to eat or swallow solid foods, his diet consists of strained foods fed by gastrostomy. Barium swallow and fluoroscopy of the trachea showed no apparent physiological reason for this persistent problem with swallowing. His current medications include chlorothiazide and spironolactone for treatment of chronic cor pulmonale.

Discussion

Remote radiofrequency diaphragm pacing has been used successfully in the treatment of adults with chronic ventilatory insufficiency with normal functioning phrenic nerves and diaphragm. Such patients include those with paralysis of respiratory muscles, with acquired central hypoventilation syndrome, and with chronic obstructive pulmonary disease.³ In infants and children however, unilateral pacing is not feasible because of the wide mediastinal shift which occurs with excursion of only one dia-

phragm on stimulation of the unilateral phrenic nerve. Consequently, bilateral diaphragmatic pacing is used, but only during sleep.

Long-term results of intermittent, bilateral diaphragmatic pacing are not known because of the small number of cases reported. The longest duration of successful intermittent bilateral pacing reported thus far in a child with CCHS is nearly 3 years (C E Hunt, 1979, personal communication). Radecki and Tomatis reported continuous bilateral pacing of an infant with bilateral phrenic nerve paralysis for 142 days before death from bronchopneumonia.² Initial histopathological examination of sections of a phrenic nerve from that infant showed no abnormalities. However, subsequent evaluation of those same specimens showed axonal dystrophy at the site of the electrode implantation and more severe distal degeneration.⁴ Continuous bilateral pacing is undesirable; it is also unnecessary unless both voluntary and involuntary control of respirations are deficient. Our patient does not hypoventilate while awake, thus avoiding the need for continuous pacing.

The problems associated with bilateral phrenic nerve pacing in infants and children are related more to cor pulmonale, a result of chronic hypoventilation, than to the mechanics of pacing itself. Important ancillary management of our patient includes supplemental oxygen, diuretics, and meticulous attention to pulmonary toilet, tracheostomy care, and reduction of environmental particulate matter. Upper airways occlusion by secretions is a significant risk in any patient with a tracheostomy.

The long-term prognosis for our patient is uncertain. CCHS appears to be a permanent defect in voluntary regulation of sleep, perhaps a congenital defect in central nervous system development. In one patient with CCHS a generalised decrease in the density of neurons and myelinated nerve fibres in the respiratory centres of the medulla was found at necropsy.⁴ However, this patient had had neither voluntary nor involuntary control of ventilation. Custer *et al.*⁵ reported improvement in ventilatory responses to CO₂ over a period of 9 months in a patient with CCHS. Despite the uncertainty regarding the longevity of our patient, successful diaphragmatic pacing has enabled him to become independent of mechanical ventilation and to lead a relatively normal life.

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Neonatal systemic candidiasis treated with miconazole

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SUMMARY Two premature newborn infants with systemic candidiasis are reported; both were treated with miconazole. One died and the other made a complete recovery. Miconazole may be a useful addition to the drugs available for the treatment of systemic candidiasis in the neonate, but all of them have serious limitations.

Systemic candidiasis is recognised as a potential hazard in premature newborn infants receiving intensive care. Effective treatment can be given for this condition, and it is therefore important to make the diagnosis early. This paper reports 2 infants; both were treated with miconazole but one died.

Case reports

Case 1. A boy, birthweight 950 g, was born preterm in the antenatal ward in January 1979. His mother had been given dexamethasone and salbutamol since her admission in premature labour 4 days earlier. Gestational age was estimated at 27 weeks, and the baby was transferred to Hammersmith Hospital 4 hours after birth.

He developed clinical and radiological evidence of hyaline membrane disease. The first examination showed no other abnormality, although subsequent abdominal palpation suggested the possibility of a horseshoe kidney. An umbilical arterial catheter was inserted to monitor blood-gases, which remained satisfactory in ambient oxygen concentrations below 60%.

At age 8 hours the baby started having apnoeic attacks. Initial investigations did not suggest an underlying cause other than immaturity. He was treated with penicillin and gentamicin for 7 days.

Continuous positive airways pressure (CPAP) proved unhelpful, but continuous intravenous infusion of aminophylline resulted in considerable diminution of the frequency and severity of his apnoeic attacks.

He was fed intravenously via Silastic central venous cannulas from 5 to 34 days of age. Nasojejunal feeds were introduced at 11 days, but were stopped at 14 days because of recurrence of apnoeic attacks. At this stage there was hypercapnia, associated with excessive tracheal secretions, and the baby received respiratory assistance, in the form of intermittent positive pressure ventilation (IPPV) and CPAP, from 16 to 24 days of age. A second course of penicillin and gentamicin was given for 11 days. *Staphylococcus epidermidis* and *Streptococcus viridans* were isolated from a pharyngeal swab on day 24, but no pathogens were isolated from repeated blood cultures, the Silastic cannula tip, cerebrospinal fluid (CSF), or urine specimens.

Thereafter progress was satisfactory until the 29th day, when, during the introduction of a nasojejunal tube, he again had an apnoeic attack, and he appeared pale and inactive. Investigations showed: haemoglobin 10.5 g/dl, WBC $29.5 \times 10^9/l$ (71% neutrophils, 7% bands). CSF contained 4 RBC and $20 \text{ WBC} \times 10^6/l$, but no organisms were seen or cultured. Blood cultures yielded *S. epidermidis* from one bottle and nonhaemolytic streptococcus from one bottle.

He was given a third course of penicillin and gentamicin, and his condition improved. Nasojejunal feedings were introduced gradually, until by day 34 he was entirely milk fed and the central venous feeding cannula could be removed. *S. epidermidis* was subsequently cultured from the catheter tip.