Mask ventilation in the early management of congenital central hypoventilation syndrome

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Congenital central hypoventilation syndrome (CCHS) is a rare disorder of breathing which is due to abnormal autonomic control; it is characterised by alveolar hypoventilation that is most marked during non rapid eye movement sleep.[1] This condition has been linked to autonomic nervous system dysregulation, and affected children may manifest other autonomic abnormalities such as Hirschsprung's disease. It usually arises as a new genetic mutation, but an autosomal dominant inheritance has been suggested in some cases.[2] Although the first case was reported as early as 1970,[3] delays still occur in diagnosis because of its rarity and poor recognition by paediatricians.

The diagnosis is usually made for an infant who remains ventilator-dependent by exclusion of neuromuscular, lung and cardiac problems. More recently, polyalanine expansion mutation of paired-like homeobox 2B (PHOX2B) genes located on chromosome 4p12 has been identified in >90% of affected children.[2] Traditionally, as soon as the diagnosis is made, affected infants undergo tracheostomy to facilitate long-term invasive ventilatory support.[4] These children tend to stay in hospital for several months after the initial diagnosis in order to optimise ventilatory support and while awaiting organisation of appropriate community care. Home support includes provision of qualified nurses or trained carers to look after the children, especially those being invasively ventilated via tracheostomy. Children need life-long ventilatory support in the community, usually only at night, but in the most severe cases 24 h/day. The condition therefore has a considerable impact on resources.

The paediatric department at the University Hospital of North Staffordshire, Stoke on Trent has one of a small number of paediatric sleep study centres in the UK and manages children with a wide range of sleep-related breathing disorders, including CCHS. In recent years, 15 children with CCHS with a variety of ventilatory support systems such as intermittent positive pressure ventilation (IPPV) via tracheostomy, negative extrathoracic pressure tanks and non-invasive positive pressure ventilation (NIPPV) by face or nasal mask have been managed. We previously reported how negative extrathoracic pressure ventilation can help to avoid tracheostomy soon after diagnosis.[5] However, the equipment is bulky and non-mobile and can exacerbate any tendency to upper airway collapse in CCHS. With improved availability of non-invasive positive pressure ventilators and masks, we have moved from negative pressure ventilation to mask ventilation.

In the last few years, we have gained increasing experience with NIPPV, still avoiding the need for tracheostomy. In addition, we have transferred patients who were on other modes of ventilatory support to NIPPV. The success of NIPPV and responses of patients and their families has meant that this is now the preferred mode of ventilatory support for all our patients, irrespective of their age. Compared with invasive ventilatory support via tracheostomy, mask ventilation appears to be less labour intensive and associated with fewer complications. We therefore report our experience with this ventilatory modality.

PATIENTS AND METHODS

Patients

We have received 17 referrals from a wide geographical area (including one from abroad) the oldest patient being 21 years old now. One child was referred for a second opinion and one child died at the age of 2 years from a non-respiratory complication; these are therefore excluded from the study. Thus the study population consists of 15 children (five boys and 10 girls) with a median age of 13 years (range 9 months–21 years).

The diagnosis was made or suspected during early infancy in all the children except two. It was made at 2 years in one child when weaning from the ventilator became difficult after intubation for a bronchiolitis-like illness. In another child, the diagnosis was suspected at 14 months when all other possibilities were excluded.

In our institution, the diagnosis is now based on the following:

1. Clinical symptoms, such as a history of recurrent apnoea, shallow breathing, or oxygen desaturation or hypercapnia noted particularly while the child is asleep, or a history of an affected sibling.
2. Sleep study, with confirmation of sleep–wake state-related hypoventilation, baseline hypoxaemia, breath-by-breath hypoxaemic episodes.
3. Exclusion of metabolic and neuromuscular disorders (eg, myasthenia gravis), congenital cardiac problems or an identifiable brainstem lesion that could account for the alveolar hypoventilation.
4. Genetic testing: assay of the PHOX2B polyalanine repeat mutation is a highly sensitive and specific test for confirming the diagnosis of CCHS.[2] In our cohort, 14 children have already been tested, and 13 were found to be positive for the PHOX2B mutation. Extended genetic testing has been requested for one child in whom it was negative. Identification of this mutation has not only hastened the diagnosis, but also avoided detailed investigations for metabolic and neuromuscular diseases. In addition to early diagnosis, the length of the repeat mutation may provide an indication of the severity of the CCHS phenotype.[2 6] In the case of one of our affected patients, the mutation has also been found in another affected sibling and mildly symptomatic mother, suggesting an autosomal dominant inheritance.[7] Currently, we routinely offer genetic testing to the entire family, to identify asymptomatic/mildly affected members, and also genetic counselling.

Methods

The case notes of all 15 children were examined to determine the ventilatory strategy used for them since the time of referral. In addition to the various ventilation methods, we determined the time taken to fully establish mask ventilation and the problems encountered and

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Table 1 Details of patients in whom mask ventilation was established at a later age

No	Ventilatory support at referral	Age at referral	Age at onset of mask ventilation (years)	Current age (years)
1	NPV	4 years	8	21
2	PPV via tracheostomy	4 weeks	9	19
3	PPV via tracheostomy	4 weeks	11	19
4	NPV	12 weeks	3	18
5	PPV via ETT	2 years	9	15
6	PPV via ETT	4 weeks	2	14
7	None	10 weeks	9	14
8	PPV via tracheostomy	14 months	3	13
9	PPV via ETT	8 weeks	1.5	11

ETT, endo tracheal tube; NPV, negative pressure ventilation; PPV, positive pressure ventilation.

subsequent side effects or complications of mask ventilation.

A questionnaire was sent to all nine patients/parents who had received alternative forms of ventilation (IPPV via tracheostomy and/or negative pressure ventilation) before being tried on mask ventilation. The questions asked about various aspects of ventilatory support since the diagnosis was made, their opinion about mask ventilation compared with previous mode(s) of ventilation, and their opinion of the advantages and disadvantages. Completed questionnaires were returned by all.

As this was a review of clinical practice, approval from the local research ethics committee was not sought.

RESULTS

Until 1996, there were nine patients under our care, and our ventilatory strategy was to introduce negative pressure ventilation whether or not tracheostomy had been performed. Mask ventilation was later added to negative pressure ventilation, and, if the child was old enough to tolerate this, he/she was gradually weaned from negative pressure ventilation, allowing management with mask ventilation alone. If the child had a tracheostomy, they would be decannulated over the course of the next few months.

It took a median duration of 3 years (range 1.5–9) to totally wean these children from negative pressure ventilation to mask ventilation at a median age of 8 years (range 1.5–11) (table 1). In the three patients who had a tracheostomy in place, decannulation was performed at 3, 9 and 11 years. In one patient, establishment of mask ventilation was delayed because of development of significant subglottic stenosis after tracheostomy. The length of time to adjust to mask ventilation varied between zero and a few months, but in most children (seven out of nine) it was less than a week.

In the last few years, improvements in the design of face and nasal masks and the introduction of novel non-invasive ventilators that can be used even in small infants have prompted us to initiate mask ventilation as the first choice ventilatory support, aiming, if possible, to avoid the need for tracheostomy or negative pressure ventilation. Since 1996, we have received six referrals for whom the diagnosis of CCHS was confirmed; all were less than 6 months of age at the time of referral. All these children were started on mask ventilation soon after admission and tolerated it well (table 2). When we asked the parents how long they felt it took for their baby to adjust to mask ventilation, all except one answered less than a week.

Therefore in our current case load of 15 children, full-mask ventilation was established at a later age (median 8 years, range 1.5–11 years) in nine children and at an early age in six children (median 8 weeks, range 5–26 weeks).

The questionnaire survey confirmed that all the parents and/or children felt that mask ventilation was preferable to either tracheostomy or negative pressure tanks. The reasons included no need for suction, ease of transport, better sleep pattern, more efficient ventilation (lower carbon dioxide and stable oxygen saturation levels), and higher level of confidence in the child because he/she looks ''normal''. There was no correlation between the age at which a mask was first tried and the time taken to adjust to it.

Despite its advantages, the use of mask ventilation in young children over a long period is not without problems. Table 3 gives an overview of the complications we have encountered in our patient group.

Table 2 Details of patients in whom mask ventilation was started at an early age

No	Ventilatory support at referral	Age at referral (weeks)	Age at onset of mask ventilation (weeks)	Current age (years)
1	PPV via ETT	5	8	11
2	None	2	5	8
3	PPV via ETT	4	7	7
4	PPV via tracheostomy	26	26	2
5	PPV via ETT	5	12	1.5
6	PPV via ETT	5	7	1

ETT, endo tracheal tube; NPV, negative pressure ventilation; PPV, positive pressure ventilation.

DISCUSSION

We have no data available on the annual incidence or prevalence of this disorder in the UK, although Jardine *et al*[8] reported 18 cases of CCHS from a UK-wide survey in 1999. The most robust published data on the incidence of CCHS are from the French Congenital Central Hypoventilation Registry, which estimates an incidence of 1 per 200 000 live births in France.[9] They have also identified a significant increase in recent years compared with the 1980s. If these figures are extrapolated to the UK population, there would be at least four newly diagnosed cases every year and 60–70 affected children. Recently, genetic tests confirmed CCHS in five adults who all had mild symptoms in childhood and survived to adulthood without artificial ventilatory support until the time of diagnosis.[7] Therefore, we believe that, with wider availability of genetic testing, the number of children with CCHS is likely to increase. Although, the absolute number of children with CCHS is not large, they consume substantially more resources in both equipment and carers than required for many other long-term paediatric illnesses. Most importantly, the overall outcome for these children is generally good with appropriate ventilatory support and monitoring. Although we have previously used ventilation via tracheostomy and subsequently negative extrathoracic pressure, we have found that mask ventilation is feasible, effective and accepted in infants with CCHS.

Traditionally, tracheostomy has been performed as an elective procedure under general anaesthesia in children with CCHS. Although generally a safe technique, there are a number of longer-term complications associated with it, including delayed speech and language development,[10] colonisation and infection of the lower respiratory tract, and tracheal

Table 3 Complications encountered from long-term mask ventilation in congenital central hypoventilation syndrome (total number of patients = 15)

Complication	No of patients	Comments
Redness/marking of the skin	12	One child developed small scar on the bridge of the nose
Orthodontic problems	6	In one child, changing to nasal cushions prevented further progression
		In five children, no major problems, but under regular orthodontic review
Abdominal distension with wind	1	
Bad breath	1	

granulations and stenosis. In addition, the most common causes of tracheostomy-related death are cannula obstruction and accidental decannulation.[11] For example, in one study, 33% of patients had excessive granulation tissue, and there was a tracheostomy-related death rate of 4%.[12] Tracheostomy also limits the ability of children to partake in swimming activities, although swimming is something that should be undertaken with caution, given the ability of children with this condition to hold their breath for long periods underwater without experiencing the sensation of asphyxia (personal observations).

Children who require ventilatory support via tracheostomy usually need full-time carers in their first few years, and organising this leads to a substantial delay in hospital discharge. However, children receiving mask ventilation are less dependent on carers, especially during the day time, and thus hospital discharge can be expedited. In addition to early discharge, there are significant differences in the cost of looking after children at home depending on their ventilator dependency. For example, the average estimated annual cost of looking after a child with complex ventilator dependency (ie, needing 24 h carers) is £127 109, which compares favourably with the £17 876 annual cost for a child who has simple ventilator dependency (ie, mask ventilation only at night).[13]

Despite these disadvantages, an epidemiological survey involving 196 patients with CCHS from 19 countries has shown that more than 60% of children with CCHS are still ventilated via tracheostomy.[14]

To avoid the complications of invasive ventilation, we have used non-invasive means of providing ventilatory support, initially in the form of negative pressure ventilation, and, since 1996, with NIPPV. This does not have the disadvantages of negative pressure ventilation or invasive ventilation. Masks are relatively easy to apply and parents can be trained over a shorter period to manage effectively with little assistance. Our questionnaire survey confirmed that the parents and older children preferred mask ventilation to negative pressure ventilation or tracheostomy. It enabled them to travel freely and with less intrusion into their family life.

In younger infants, the main initial challenge was selection of an appropriate mask and means of securing this effectively so that ventilation was possible without causing pressure sores or excessive leakage. It was also important to ensure that the airway was maintained by correct head positioning. Sometimes this was facilitated by the use of a neck roll. Despite these challenges, all six infants tolerated mask ventilation without major problems from the outset. Parents were involved early in learning to check mask position and fitting and airway positioning and ensuring effective chest movement. This was supported by continuous monitoring of the pulse oximeter (oxygen saturation) and transcutaneous carbon dioxide. These provide early indications of inadequate ventilation; it usually became apparent that infants who managed with adequate oxygen saturation in room air (>94%) were likely to be effectively well ventilated and maintaining normal lung volumes. However, parents became used to relying on transcutaneous carbon dioxide measurements, which were one of the earliest signs of intercurrent infection. It also allowed care plans to include some manipulation of ventilator rates and pressures at home, before hospitalisation was sought.

Once the infant was established on mask ventilation, known long-term complications were monitored and prevented if possible.[15] The most common complication was marking of the skin, which may lead to ulceration if left unattended. It was important to stress the need for close monitoring and care to be taken to prevent skin ulceration by the use of appropriate mask fittings and strap tightness, and the early use of barrier dressings, as once the skin is eroded it can be difficult to apply the mask. This was impressed on parents and carers at the outset. In our patient population, no child needed intubation because of skin breakdown.

Impairment of facial growth resulting in mid-face hypoplasia (where the maxilla fails to advance with the growth of the mandible) and dental malocclusion is an important and well-recognised complication of long-term use of mask ventilation in children from any underlying cause.[16 17] The severity of this complication can be reduced by alternating between face masks, nasal masks and nasal pillows, use of customised masks, and avoiding tight fitting.[18]

There are only a few published case reports in children with CCHS, involving one or two children, on the use of long-term mask ventilation from early infancy.[19–21] Tibballs and Henning[19] reported development of class 3 dental malocclusion in both their patients after about 2 years. They therefore added negative pressure ventilation to reduce the duration of mask ventilation. Villa *et al*[17] described successful correction of mid-face hypoplasia with an orthodontic device in a 7-year-old child who had been ventilated with a nasal mask from the age of 9 months for CCHS.

In our cohort, six parents mentioned problems with facial morphology mainly in the form of overbite (table 3); none of them yet required any intervention. However, our report is not prospective, and we do not offer regular orthodontic review of patients. Therefore the severity of mid-facial hypoplasia may not be properly assessed in our older patients. Assessment of any potential problems with facial growth will require longer-term follow-up, as facial growth is not yet complete. The oldest child in our study group in whom mask ventilation was started in early infancy is now 11 years old, and, although under regular orthodontic observation, he does not yet need intervention.

PHOX2B is expressed in the dorsal rhombencephalon, which also gives rise to facial structures. A recent study on the facial morphology of patients with CCHS[22] suggested a characteristic facial phenotype in which the faces of children and young adults with PHOX2B-confirmed CCHS were shorter and flatter, with inferior inflection of the lateral segment of the vermillion border on the upper lip and a characteristic box-like shaped face. These facial features appear to be independent of the effect of mask ventilation. Therefore it is possible that problems with mid-face hypoplasia are due to CCHS itself; however, early

recognition and regular orthodontic assessment are highly recommended.

Other reported complications include claustrophobia, difficulties with excessive airway secretions, and abdominal distension caused by air swallowing.[23] The nasal mask reduces the incidence of most of these complications by reducing the area of contact between the face and mask. All except one of our patients are currently being ventilated by nasal mask.

There are situations where it is not practical to ventilate a child by a mask—for example, if ventilatory support is needed for 24 h a day (eg, 10% of the 196 patients in the survey of Vanderlaan *et al*[14]). All 15 children under our care are only ventilated during sleep. In children with severe learning difficulties and those with swallowing difficulties, mask ventilation may not be the ideal mode of ventilatory support. In such cases, alternative modes of ventilatory support need to be considered. In our cohort, two children presented with hypotonia, which, in fact, improved after introduction of mask ventilation. Another child had severe autism, and one had mild motor and speech delay. Mask ventilation was accepted by all four children without any difficulty.

CONCLUSIONS

Mask ventilation can be considered in most patients presenting with a diagnosis of CCHS in early infancy. It is effective, cheaper than other methods, and preferred by both patients and their parents. Children who already have other modes of ventilatory support can be successfully weaned on to mask ventilation within a short period of time. There are cases, however, in which mask ventilation may be difficult and alternative modes of ventilation, such as negative pressure ventilation, positive pressure ventilation via tracheostomy or phrenic nerve pacing, need to be considered.

Competing interests: None.

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Extremely preterm births: recommendations for treatment in European countries

Maria S Pignotti

With the advances in medical technology, the outcome for high-risk infants has greatly improved, and the limit of human viability has shifted towards an increasingly lower gestational age. However, hand in hand with the positive outcome of saving neonates, modern neonatal intensive care has also brought to light several issues of an ethical nature in the care of these infants, especially those considered to be affected by incurable diseases or severely injured during pregnancy, delivery or the early neonatal period, those affected by major and/or multiple congenital abnormalities, and those at the borderline of viability (25 or fewer completed weeks of gestation). The survival rate of extremely preterm infants improved in the early 1990s, largely as a result of greater use of surfactant therapy and antenatal corticosteroids. However, this improvement in survival may not have been associated with a proportionate decrease in morbidity.[1–10] Chronic lung disease, sepsis and poor growth are still common, the neurodevelopmental outcome and

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