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BRIEF REPORT

Strategy of changing from tracheostomy and non-invasive mechanical ventilation to diaphragm pacing in children with congenital central hypoventilation syndrome

Congenital central hypoventilation syndrome (CCHS) is a rare disorder that affects central control of breathing, and paediatric treatment varies worldwide.[1] One approach is diaphragm pacing (DP), by phrenic nerve stimulation or direct diaphragm muscle stimulation, with or without a tracheostomy.[2]

In Sweden, non-invasive ventilation (NIV) has been the first-line ventilator support for patients with CCHS.[3] However, disadvantages such as midface hypoplasia and unintentional leakage have required assessment over time.[4]

Diaphragm pacing implants are provided at the National Reference Center for Diaphragm Pacing at Uppsala University Hospital, Sweden, at 3–4 years of age, when the upper airways have become more stable. Some international centres wait until children are older.[2]

Our aim was to evaluate switching patients with CCHS from mechanical ventilation, namely tracheostomy or NIV, to DP.

We retrospectively studied 23 patients with central hypoventilation conditions who underwent DP implantation at the Hospital between 1 January 1980 and 31 December 2020. They included 12 international referrals. CCHS was defined as central hypoventilation with failed respiratory control, mainly during sleep. This was confirmed by gene testing and included paired-like homeobox 2b and other genetic mutations.[1] A successful transition to DP was defined as a complete change to sleep-assisted, non-mechanical ventilation.

All patients accepted for DP implantation needed respiratory support, verified by cardiorespiratory and polygraphic monitoring and clinical observation. Upper airway patency was evaluated before surgery was performed.

This study comprised 23 patients (13 female) with central hypoventilation conditions, who received DP at a mean age of 9.1 years (range 2.9–31.2) (Table 1). They included 21 with CCHS, and 18/23 were using NIV at the time of implantation. Five patients had a tracheostomy before implantation, and they were all decannulated after surgery: one within 3 months and 4 after 3–6 months. We found that 20/23 were successfully transferred to DP and 3 continued with NIV. Some patients have now been using DP for 30 years without needing replacement electrodes or receivers.

Four Swedish patients with CCHS were not included because they were under 3 years of age and ineligible for DP implantation, but they will be considered when they reach 3 years of age.

Of the 23 patients, 18 had PHOX2B gene mutations: one had a 20/24 polyalanine repeat expansion mutation (PARM), two had a 20/25 PARM, six had a 20/26 PARM, five had a 20/27 PARM, two had a 20/30 PARM, one had a 20/33 PARM and one had a non-PARM mutation. One had rapid-onset obesity with hypothalamic dysregulation, hypoventilation and autonomic dysregulation. One tested negative for paired-like homeobox 2b, and three tested positive, but with unknown genotypes (Table 1).

Most patients were successfully ventilated with DP, in line with earlier studies.[2,5] Our cervical approach to DP implantation was feasible and minimally invasive, with low morbidity.

We believe this is the first study to demonstrate that ventilator support in children with CCHS may shift from NIV to DP at an early age. This could prevent midface deformation after long-term NIV use.

In our experience, younger patients accept DP better and older patients need a longer adaptation period. The age limit of 3–4 years has been set due to increased stability of the upper airways and larger patient size, which simplifies surgical access. Young children seem to be more sensitive to upper airway obstruction because they lack synchrony between upper airway skeletal muscles and the diaphragm.[2] Upper airway collapses and obstructive apnoeas were prevented by applying lower DP amplitude settings and higher frequency rates. This even worked for patients with upper airway obstruction due to midface deformation prior to DP implantation. A novel observation was that all patients who had a tracheostomy were decannulated and able to exclusively rely on DP for ventilatory support. Decannulation was determined by the ear, nose and throat

Abbreviations: CCHS, congenital central hypoventilation syndrome; DP, diaphragm pacing; NIV, non-invasive ventilation; PAR, polyalanine repeat expansion mutation.

TABLE 1 Demographics of the 23 patients with central hypoventilation conditions who received diaphragm pacing

Gender	Diagnosis	PHOX2B/other gene mutations	Co-morbidity	Before DP	Age at operation (years)	Age in December 2020 (years)	Current DP use
M	CCHS	20/26		NIV	2.9	3.8	Sleep
F	CCHS	20/26		NIV	3.4	4.6	Sleep
F	CCHS	20/25		NIV	3.7	14.5	Sleep
F	CCHS	Unknown		Trach	3.8	14.6	Sleep
M	CCHS	20/27	Hirsch	NIV	3.8	11.9	Sleep
M	CCHS	20/30		Trach	4.6	5.4	Sleep
M	CCHS	20/27	SSS	Trach	4.7	11.6	Sleep
M	CCHS	20/26		Trach	4.7	10.0	Sleep
F	CCHS	20/26		NIV	4.9	11.0	Sleep
F	CCHS	20/27		NIV	5.1	19.5	Sleep
M	ROHHAD	Not PHOX2B		NIV	5.8	15.5	Sleep
F	CCHS	20/33		NIV	6.4	15.1	Sleep
M	CCHS	20/27		NIV	6.8	13.0	Sleep
F	CCHS	20/26		NIV	8.0	39.9	Not used
F	CCHS	20/27		NIV	8.3	17.2	Sleep
M	CCHS	Unknown		NIV	8.4	40.5	Sleep
M	CCHS	Unknown		NIV	9.3	12.1	Sleep
F	CCHS	NP		Trach	13.2	14.8	Sleep
F	CCHS	20/26	SSS	NIV	15.1	27.0	Sleep
M	CCHS	20/30	SSS	NIV	17.2	20.9	Not used
F	CCHS	20/25		NIV	18.3	24.8	Not used
F	Not CCHS	Negative PHOX2B		NIV	19.7	21.0	Daytime
F	CCHS	20/24		NIV	31.2	32.1	Sleep

Note: Mean age in years at DP implantation (9.1, range 2.9–31.2), at the end of the study (17.4, range 3.8–40.5) and at tracheostomy decannulation (6.2, range 3.8–13.2).

Abbreviations: CCHS, congenital central hypoventilation syndrome; DP, diaphragm pacing; F, female; Hirsch, Hirschprung's disease; M, male; NIV, non-invasive ventilation; NP, non-polyalanine repeat expansion mutation; PHOX2B, paired-like homeobox 2b; ROHHAD, rapid-onset obesity with hypothalamic dysregulation, hypoventilation and autonomic dysregulation; SSS, sick-sinus syndrome; Trach, tracheostomy.

surgeon in each case. We suggest that decannulation can be planned when adequate ventilation is achieved by DP. This should be carefully evaluated with polygraphic monitoring.

Three-month and annual follow-ups were performed on the cohort at the reference centre or local clinics. These included objective measures for evaluating DP ventilation, such as clinical evaluations with carbon dioxide and/or polygraphic monitoring. A limitation of our study may have been that we could not follow up overseas patients. However, their respective hospitals have reported that they are doing well.

Diaphragm pacing seems to be a feasible treatment option for patients with CCHS. Most of our CCHS patients were satisfied with their DP and were able to stop using mechanical ventilation altogether. DP maintained adequate ventilation and increased daily comfort.

CONFLICT OF INTEREST

None.

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