Clinical Investigations

Respiration

Respiration
DOI: 10.1159/000381401

Received: July 28, 2014
Accepted after revision: March 3, 2015
Published online: April 25, 2015

Diaphragm Pacing without Tracheostomy in Congenital Central Hypoventilation Syndrome Patients

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Key Words
Diaphragm pacing · Congenital central hypoventilation syndrome · Tracheostomy · Decannulation · Upper airway obstruction

Abstract
Background: Congenital central hypoventilation syndrome (CCHS) is a rare disorder affecting central control of breathing. Thus, patients require lifelong assisted ventilation. Diaphragm pacing (DP) may permit decannulation in those who are ventilator dependent only during sleep. ***Objective:*** The purpose of this study is to determine if patients with CCHS can be successfully ventilated by DP without tracheostomy. ***Methods:*** We reviewed the records of 18 CCHS patients (mean age 19.5 ± 10.1 years; 44% female) who were ventilated by DP only during sleep. ***Results:*** Prior to diaphragm pacer implantation surgery, 14 CCHS patients had been using home portable positive pressure ventilation (PPV) via tracheostomy, 1 had been on PPV via endotracheal tube, and 3 had been using noninvasive PPV (NPPV). Of the patients with tracheostomy prior to DP (n = 15), 11 (73%) were decannulated and ventilated successfully by DP without tracheostomy. Of all the patients reviewed (n = 18), 13 (72%) were successfully ventilated by DP without tracheostomy. Obesity prevented successful DP without tracheostomy in 1 patient, and upper airway obstruction prevented success in another patient. Snoring and/or obstructive apneas were present in some patients, but they were improved by diaphragm pacer changes, adenotonsillectomy, and/or use of nasal steroids. ***Conclusions:*** DP without tracheostomy can be successfully achieved in patients with CCHS. Snoring and obstructive apneas, when present, can be managed by diaphragm pacer changes and medical therapies. Obesity can pose a challenge to successful DP.

Introduction

Congenital central hypoventilation syndrome (CCHS) is a genetic disorder with failure of central control of breathing and of the autonomic nervous system due to a mutation in the PHOX2B gene [1–5]. Affected patients usually present in infancy with absent or negligible ventilatory sensitivity to hypercapnia and hypoxemia that is worse during sleep than wakefulness. They require lifelong assisted ventilation during sleep or 24 h a day [1, 2, 5]. Most patients receive assisted ventilation using positive pressure ventilation (PPV) via tracheostomy [1, 2,

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5–9]. Some families choose to use ventilatory support without a tracheostomy, such as noninvasive PPV (NPPV) [9–14], diaphragm pacing (DP) [8, 9, 15–19], or negative pressure ventilators [9, 20]. DP via phrenic nerve stimulation has been used for over four decades in infants and children [15–18]. It allows full-time ventilator-dependent CCHS patients to be free of PPV during the day, allowing mobility and independent living. In those who are ventilator dependent only during sleep, DP may permit decannulation of the tracheostomy.

There are currently no published data on the successful outcome of DP without tracheostomy in CCHS patients who are ventilator dependent only during sleep. Thus, we performed this retrospective study of CCHS patients who underwent DP implantation surgery. We hypothesized that many CCHS patients who are ventilator dependent only during sleep can be ventilated successfully without tracheostomy by DP.

Methods

The Children's Hospital Los Angeles (CHLA) follows 51 CCHS patients, 23 of whom have received diaphragm pacers. We reviewed the records of the 19 CCHS patients who were ventilator dependent only during sleep and received DP at the CHLA from January 1980 to January 2013. The diagnosis of CCHS was confirmed by genetic testing in 16 patients. One patient was excluded as he was lost to follow-up. Therefore, data on the remaining 18 patients are reported.

CCHS patients who were ventilated by DP during sleep were reviewed for the following information: (1) age, (2) type of assisted ventilation prior to DP (NPPV or PPV via tracheostomy), (3) time from diaphragm pacer surgical implantation to initiation of pacing, (4) time from DP initiation to all-night DP, (5) time from DP surgery to decannulation, (6) obstacles to decannulation, and (7) interventions to improve ventilation via DP. Successful transition to DP was defined as complete transition to assisted ventilation during sleep via DP without tracheostomy.

This study was approved by the Institutional Review Board of the CHLA.

Results

Patient Characteristics

Eighteen patients were included in the study, 44% female, with a mean age at diaphragm pacer implantation of 9.6 ± 6.4 years (range 1.5–23.5). PHOX2B mutations were confirmed in 16 patients. Ten patients had a 20/25 polyalanine repeat expansion mutation (PARM), 1 patient had a 20/26 PARM, 3 patients had a 20/27 PARM, 1 patient had a 20/33 PARM, and 1 patient had a novel p.82 mutation. Two patients were not tested. The body mass index (BMI) and BMI z-scores (for patients 5–19 years old during their clinic visit) were calculated for each patient. Two patients were overweight and 2 patients were obese based on cutoffs by the World Health Organization. All patients in our study required assisted ventilation only during sleep. The patients' characteristics are listed in table 1.

Mode of Ventilation Prior to DP

Prior to diaphragm pacer implantation surgery, 14 patients had received assisted ventilation using home portable PPV via tracheostomy. One patient never had a tracheostomy, since she had been on mechanical ventilation via endotracheal tube until she was 17 months old, which was when the diaphragm pacers were initially placed. Two patients were already decannulated, and they had used NPPV via nasal mask prior to surgery. One patient had her tracheostomy already capped while she was awake and asleep and had been receiving NPPV via nasal mask prior to her evaluation for DP.

Outcome following Diaphragm Pacer Surgery

Seventeen CCHS patients had diaphragm pacer implantation surgery at the CHLA. There were no major intraoperative complications. One patient had already been receiving DP prior to transferring her care to the CHLA. All patients received the Mark IV (Avery Biomedical Devices, Inc.) diaphragm pacer system with intrathoracic placement of electrodes. The majority had their diaphragm pacers implanted thoracoscopically as described by Shaul et al. [20].

The mean age at DP implantation was 9.6 ± 6.4 years (range 1.5–23.5), with the youngest patient undergoing implantation surgery at 17 months of age. DP was initiated at a mean of 2.8 ± 2.2 months (range 0.5–10.2) following surgery. Sixteen of the 18 patients (89%) achieved full nighttime DP after initiation at a mean of 6.6 ± 7.5 months (range 2.5–32.5) from surgery. One patient was on full nighttime DP after 3 years, as he and his family opted to use DP only when a nurse was present.

Eleven (73%) of the 15 patients with tracheostomy prior to DP were decannulated successfully. Thirteen of the total of 18 patients (72%) were successfully ventilated by DP without tracheostomy. One patient who had been receiving nasal NPPV but had a tracheostomy was decannulated 2 weeks after the pacer implantation surgery. The mean age at decannulation was 12.6 ± 7.1 years (range 5.2–28.4). Decannulation was performed at a mean of 12.2 ± 11.0 months (range 0.6–40.6) from diaphragm pacer implantation surgery. One patient's values were not included in the calculation of the mean. He had develop-

Table 1. Outcome following diaphragm pacer implantation surgery

Patient No.	Age at pacer implantation, years	Sex	PHOX2B mutation	BMI	BMI z-score	Ventilatory support prior to DP	Pacer implant to init.,[a] months	Init. to full nighttime pacing,[b] months	Pacer implant to decann.,[c] months	Current age, years	Current status
1	1.5	F	20/25	24.0	–	PPV/ETT[d]	0.5	3.0	–	36.1	pacing without trach.
2	3.2	M	20/25	29.1	–	PPV + trach.[e]	1.5	3.0	302.5	35.7	pacing without trach.
3	3.5	M	20/27	14.5	–0.99	PPV + trach.	10.2	3.0	40.6	6.3	pacing without trach.
4	4.1	M	20/25	14.2	–1.08	PPV + trach.	5.1	8.3	17.9	9.4	pacing without trach.
5	4.4	M	not tested	15.5	0.08	PPV + trach.	1.5	4.1	8.7	11.7	pacing without trach.
6	4.6	F	20/25	21.4	1.27	PPV + trach.	4.6	4.2	12.8	11.3	pacing without trach.
7	4.7	M	20/25	16.4	0.61	PPV + trach.	2.2	14.1	–	10.6	PPV + trach.
8	5.1	M	20/27	15.9	0.37	PPV + trach.	2.5	6.7	–	9.4	PPV + trach.
9	5.8	M	20/25	16.0	0.41	PPV + trach.	1.2	3.6	10.9	7.2	pacing without trach.
10	9.3	F	20/25	15.5	–0.66	PPV + trach.	2.6	2.7	7.1	11.7	pacing without trach.
11	12	M	not tested	–	–	PPV + trach.	1.5	2.5	5.1	19.5	pacing without trach.
12	12.1	F	20/25	39.0	–	NPPV	2.9	6.0	–	25.9	paced for 7 years without trach., NPPV due to obesity
13	14.3	F	20/33	24.5	0.76	PPV + trach.	1.4	3.0	10.4	29.9	pacing without trach.
14	14.8	F	20/27	17.5	–0.93	PPV + trach.	2.1	4.2	7.9	23.7	pacing without trach.
15	16	F	20/25	19.5	–0.37	nasal PPV + trach. capped	2.3	5.3	0.6	20.4	pacing without trach.
16	16.6	M	20/26	19.7	–	PPV + trach.	4.8	32.5	–	31.6	pacing, chose to keep trach.
17	17.9	M	20/25	22.8	0.28	NPPV	2.3	–	–	22.6	NPPV
18	23.5	F	p.82	36.4	–	PPV + trach.	1.9	–	–	27.1	PPV + trach.
Mean	9.6±6.4			21.3±7.5	–0.02±0.77		2.8±2.2	6.6±7.5	12.2±11.0	19.5±10.1	

ETT = Endotracheal tube; trach. = tracheostomy. [a] Time from diaphragm pacer implantation to initiation of pacing. [b] Time from initiation to full nighttime pacing. [c] Time from diaphragm pacer implantation to decannulation. [d] PPV via endotracheal tube. [e] PPV via tracheostomy.

mental delay, and the patient and his family did not want him decannulated until 25 years after the diaphragm implantation. Of the patients who had a tracheostomy, all had met the criteria for pacing without tracheostomy prior to decannulation as set in our DP program at the CHLA and as noted in table 2 [16].

Shoulder pain with DP using intradiaphragmatic phrenic nerve stimulation was reported by Morélot-Panzini et al. [21]. All of our patients had intrathoracic phrenic nerve electrodes, and while shoulder pain can occur when the tidal volume is too high, the pain is relieved when the tidal volume is reduced.

Obstructive apnea can occur when DP is used without tracheostomy. In order to successfully decannulate these patients, some had to have changes in DP pacer settings (decreased tidal volume). Two patients had an adenotonsillectomy prior to decannulation. Three patients were on nasal steroids. Snoring was present in virtually all patients. Adequate ventilation was generally improved by diaphragm pacer setting changes that were performed during polysomnography.

Polysomnography

Polysomnography data were not available for all patients before and after decannulation. Only 1 patient had polysomnography data before and after decannulation. Six patients underwent polysomnography with their tracheostomy capped prior to decannulation. These patients did not show obstructive sleep apneas. Five patients underwent polysomnography after decannulation.

Of the patients who underwent polysomnography after decannulation, 1 had obstructive sleep apneas. Initially, this patient's apnea-hypopnea index was 3.4, indicating mild obstructive sleep apnea syndrome, with the lowest Sp_{O_2} 79% and the highest $P_{ET}CO_2$ 58 mm Hg. After slight adjustment of the tidal volume settings, her apnea-hypopnea index dropped to 1.7, with the lowest Sp_{O_2} 92% and the highest $P_{ET}CO_2$ 33 mm Hg.

Obstacles to Decannulation

Two patients did not achieve full nighttime pacing after diaphragm pacer surgery. One patient decided not to use pacing, since he did not like how it felt, and returned

Table 2. Criteria for pacing without tracheostomy and protocol for decannulation

Criteria for pacing without tracheostomy
CCHS requiring ventilatory support only during sleep
Not requiring daytime naps
Stable medical course requiring infrequent hospitalizations
Not requiring full-time ventilatory support during acute respiratory illnesses
Acceptance that DP is not as secure a method of ventilation and intubation may be required for serious illness
Protocol for decannulation
Establish adequate ventilation with DP using an open tracheostomy for ≥3 months
Downsize tracheostomy
Overnight polysomnography with DP and tracheostomy capped:
– if Sp_{O_2} <95% and $P_{ET}CO_2$ <40 mm Hg, consider supplemental O_2 via nasal cannula
– if OSA is present, consider decreasing tidal volume in diaphragm pacer settings, tonsillectomy/adenoidectomy, and treating nasal allergies; repeat sleep study
– if Sp_{O_2} >95% and $P_{ET}CO_2$ <40 mm Hg and no OSA is present, conduct airway evaluation by ENT; if normal, proceed to decannulation
Overnight hospital observation after decannulation

OSA = Obstructive sleep apnea.

to ventilation via NPPV. Due to obesity, 1 patient did not progress by increasing pacer usage after initiation. Her BMI was 35.8. A high amount of adipose tissue increases the distance between the antenna and the receiver of the diaphragm pacer, resulting in increased variability in the signal received by the receiver.

Obesity was an obstacle to DP in another patient who had been decannulated and had been NPPV dependent prior to DP surgery. She was doing well for 7 years with DP until she had significant weight gain (32 kg), resulting in an inability to find diaphragm pacer settings that gave adequate ventilation consistently. She had a BMI of 39. Thus, she returned to using NPPV. In our data, we consider this patient to have successfully achieved DP without tracheostomy, since she had been pacing for 7 years before her weight gain. Two other patients were considered overweight, but they did not have problems with DP. All other patients had a BMI or BMI z-score that was normal.

Four patients with tracheostomy have not been decannulated. One patient preferred to keep his tracheostomy for social reasons. One patient had severe upper airway obstruction with inspiration documented during polysomnography with the tracheostomy tube briefly removed, despite changing the DP settings, which prevented decannulation. He had normal airway examinations performed by his otolaryngologist prior to the sleep study. Decannulation was electively delayed in 1 patient due to seizures and developmental delay. As discussed previously, obesity was an obstacle in 1 patient, who was unable to progress to full nighttime pacing with tracheostomy.

Discussion

Our study shows that CCHS patients who are ventilator dependent only during sleep can be ventilated successfully by DP without tracheostomy. Most patients without comorbidities who are ventilator dependent via tracheostomy can be successfully decannulated.

Upper airway obstruction can be a complication of DP without tracheostomy [16, 22, 23]. During spontaneous breathing in normal individuals, there is synchronous contraction of the upper airway skeletal muscles with diaphragm contraction to maintain airway patency. During DP, this synchronous contraction is bypassed, predisposing the upper airways to collapse due to the negative intrathoracic pressure created by the diaphragm contraction and absent upper airway skeletal muscle contraction. Younger children and infants are more susceptible to this due to their smaller airway dimensions and the mid position of their vocal cords at rest [15, 18]. The lack of synchrony between upper airway skeletal muscles and the diaphragm has been suggested as the pathogenesis for upper airway obstruction in previous case reports. We did not conduct upper airway electromyography in our study. However, the authors cannot overemphasize the importance of assessing the upper airway anatomy by otolaryngology and performance of polysomnography with a capped tracheostomy tube prior to any consideration of decannulation. During endoscopy, the upper airway is evaluated to rule out anatomical and functional abnormalities, such as granulomas. During performance of a polysomnography with the tracheostomy capped, the diaphragm pacer settings can be adjusted to achieve optimal gas exchange, and alleviate obstructive apneas, if present, as discussed below. Even if it may not be possible to eliminate all obstructive hypopneas, DP can still be used if an adequate gas exchange is achieved.

Snoring and obstructive apneas were present in our study; however, in general, making changes in the diaphragm pacer settings alleviated these issues. We have successfully managed obstructive apneas by performing polysomnography to assess and change the pacer settings. We

decreased the tidal volume to decrease the force of inspiration with each diaphragm contraction. Some other patients responded to treating nasal allergies and/or performing adenotonsillectomy. Despite these changes, the obstructive apneas were too severe in 1 patient, so that we were unable to decannulate him. Prolonging the inspiratory time would theoretically also decrease the force of inspiration and alleviate obstructive apneas. However, in our series, we were successful by decreasing the tidal volume instead.

Obesity is an obstacle to successful DP, as seen in 2 of our patients. We attribute this to an increased distance between the antenna and the receiver resulting from large amounts of adipose tissue in the current pathway from the receiver to the antenna. Changing body positions, which can compress or increase the distance between the antenna and the receiver, may result in decreased or increased diaphragm contractions. When a patient is lying on her antenna, the fat is compressed, decreasing the distance between the receiver and the antenna, resulting in stronger diaphragm contraction. However, while lying supine, there is a greater distance between the receiver and the antenna, resulting in decreased diaphragm contraction. With obesity, there is an inability to find a consistent diaphragm pacer setting to achieve adequate ventilation. This suggests that obesity is a contraindication to DP, and weight control and counseling should be part of the initial assessment and follow-up of obese patients about to receive DP.

In conclusion, many CCHS patients who require ventilatory support only during sleep can be successfully ventilated by DP without tracheostomy. Although upper airway obstruction can occur due to the absence of synchronous upper airway skeletal muscle contraction with diaphragm contraction, changes in DP settings and other medical management can usually relieve this, facilitating tracheostomy decannulation.

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