Diaphragmatic pacing as a treatment option for congenital central hypoventilation syndrome

Rodrigo A. S. Sardenberg, Riad N. Younes

ABSTRACT

The aim of this study is to present a 15-month-old child, case of congenital central hypoventilation syndrome successfully treated by diaphragmatic pacing. The diagnosis of this syndrome depends on the documentation of hypoventilation during sleep in the absence of primary neuromuscular, lung, cardiac, metabolic disease, or an identifiable brainstem lesion. While the cause of central congenital hypoventilation syndrome is not completely elucidated, the patients have mutations of the PHOX2B gene on chromosome 4. The diaphragmatic pacemaker currently represents an excellent treatment option, and the use of this device can provide reduction in upper airway infections and quality of life improvement.
Diaphragmatic pacing as a treatment option for congenital central hypoventilation syndrome

Rodrigo A. S. Sardenberg, Riad N. Younes

ABSTRACT

The aim of this study is to present a 15-month-old child, case of congenital central hypoventilation syndrome successfully treated by diaphragmatic pacing. The diagnosis of this syndrome depends on the documentation of hypoventilation during sleep in the absence of primary neuromuscular, lung, cardiac, metabolic disease, or an identifiable brainstem lesion. While the cause of central congenital hypoventilation syndrome is not completely elucidated, the patients have mutations of the PHOX2B gene on chromosome 4. The diaphragmatic pacemaker currently represents an excellent treatment option, and the use of this device can provide reduction in upper airway infections and quality of life improvement.

Keywords: Diaphragm, Diaphragmatic paralysis, Pacemaker, Phrenic nerve

INTRODUCTION

Classical congenital central hypoventilation syndrome (CCHS), also known as Ondine’s Curse, is characterized by hypoventilation with normal respiration rates and shallow breathing during sleep with adequate ventilation during wakefulness. Severely affected individuals hypoventilate also when awake [1]. The CCHS represents an increasingly recognized group of conditions characterized by respiratory and autonomic nervous system dysregulation [2]. This rare disease was first reported in 1970 as a case report titled “Failure of Autonomic Control of Ventilation” [3], and came most visibly to the medical and public community with the American Thoracic Society (ATS) statement on CCHS in 1999 [2].

The diagnosis of CCHS is suspected due to absence of adequate ventilation during sleep, and others diseases were ruled out. While the cause of CCHS is not completely elucidated, those with CCHS have mutations of the PHOX2B gene, on chromosome 4. There are two types of disease presentation: the classic way, where the patient needs ventilatory support only during sleep (80% of cases), and the severe (20% of cases) when the patient requires ventilatory support 24 hours/day.

We report a CCHS patient with severe presentation type, successfully treated by diaphragmatic pacing.
The patient underwent general anesthesia without muscle blockers with single intubation. A staged bilateral mini-thoracotomy to access the pleural cavity was performed. The electrodes were placed underneath the phrenic nerves through careful dissection, and sutured to the pericardium by 4-0 prolene suture.

The receivers were placed in the subcutaneous tissue on the costal margin, and once they were connected to the electrodes, and they tested they showed good diaphragmatic function. The incisions were closed in layers and no chest tube was necessary. After an uneventfully recovery period, the diaphragm pacing was initiated four weeks after surgery.

Radiofrequency signals, generated by a battery-powered transmitter, were sent from an external antenna (Figure 1A), fixed to the implanted receivers (Figure 1B), which convert the radio signals into electrical impulses, causing diaphragmatic contraction.

To avoid fatigue, diaphragmatic pacing was initiated at a frequency of 15 Hz for 30 minutes during each waking hour in the first week, with increases of 30–45 minutes/week as tolerated by the patient. After 150 days hospitalization, the patient was discharged in good clinical condition, being submitted to 24 hours/day of continuous diaphragmatic pacing every day.

DISCUSSION

Congenital central hypoventilation syndrome is a rare disease—one for every 200,000 births, usually genetic in origin, resulting from a mutation in the gene PHOX2B on chromosome 4. This mutation causes a disorder in the central nervous system which leads to apnea, especially during REM sleep [2]. According to the gravity of the case, even when the individual is awake, able to maintain a satisfactory breathing on their health. As a result of hypoventilation, these individuals became hypoxemic and hypercarbic but lack the normal ventilation and arousal responses to the endogenous challenges during sleep, and the perception of asphyxia during wakefulness with and without exertion. When the disease is congenital, symptoms are present from birth, and the main symptoms are difficulty in maintaining the breathing frequency, difficulty in swallowing, cardiac arrhythmia, changes in temperature, eye disorders and gastroesophageal reflux. In 20% of patients, congenital megacolon (Hirschsprung’s disease) is present, when so called these findings Haddad syndrome.

The diagnosis of such disease is made initially with the clinical state of the patient, followed by the completion of genetic testing, which identifies the type of gene mutation and PHOX2B, therefore, more appropriate monitoring of possible malfunctions associated with the specific type of mutation, and a genetic counseling for parents who wish to have other children.

Normally, other neuromuscular diseases, cardiac and neurological disorders should be investigated. There are two types of CCHS presentation: the classic way, where the patient needs ventilatory support only during sleep (80% of cases), and the severe (20% of cases) when the patient requires ventilatory support 24 hours/day.

The diaphragmatic pacemaker currently represents an excellent treatment option.

Available for use in the US for 40 years, and released in Brazil by ANVISA in 2009. It has been used by our group in 21 patients of various etiologies, all successfully. The youngest patient implanted in Brazil—the patient in this study—was 15 months old at the time of implantation and is progressing successfully.

Figure 1: Device for phrenic nerve stimulation: (A) External parts and (B) Internal parts.
Currently around the world, some patients are pacing for 30 years, and many for 20 years. The longest pacer patient in Brazil is pacing full time for three years [4]. Diaphragmatic pacing can provide advantages to patients such as: reduction in lung infections; tracheostomy decannulation in some cases; ventilator weaning and better quality of life [4].

An upper airway evaluation is another assessment that can be helpful, specially in those where tracheostomy decannulation is being considered. Increasing the size of the upper airway with tonsillectomy and/or adenoidectomy may help minimize upper airway obstruction [5]. If the patient can sustain adequate ventilation with a small tracheostomy, the cannula may be removed [6].

Recently, a new drug treatment (desogestrel) for CCHS patients—in order to improve CO₂ chemosensitivity—was reported. One of the two patients described that without setting up the non-invasive ventilation, in this context, the benefit of desogestrel is currently conjectural [7]. Successful diaphragm pacing requires proximity to a medical team willing to maintain this system. Therefore, diaphragm pacing is an attractive alternative mode of mechanically assisted ventilation for many patients with CCHS.

Patients can lead a much more normal life by being ventilator-free, enabling them to participate in daily activities, thus improving quality of life.

CONCLUSION

Diaphragm pacing is an attractive alternative mode of mechanically assisted ventilation for many patients with congenital central hypoventilation syndrome. Patients can lead a much more normal life by being ventilator-free, enabling them to participate in daily activities, thus improving quality of life.

*********

Author Contributions
Rodrigo A. S. Sardenberg – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Riad N. Younes – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

Copyright
© 2017 Rodrigo A. S. Sardenberg et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

REFERENCES
1. Weese-Mayer DE, Rand CM, Berry-Kravis EM, et al. Congenital central hypoventilation syndrome from past to future: Model for translational and transitional autonomic medicine. Pediatr Pulmonol 2009 Jun;44(6):521–35.
2. Weese-Mayer DE, Shannon DC, Keens TG, Silvestri JM. Idiopathic congenital central hypoventilation syndrome: Diagnosis and management. American Thoracic Society. Am J Respir Crit Care Med 1999 Jul;160(1):368–73.
3. Mellins RB, Balfour HH Jr, Turino GM, Winters RW. Failure of automatic control of ventilation (Ondine’s curse). Report of an infant born with this syndrome and review of the literature. Medicine (Baltimore) 1970 Nov;49(6):487–504.

4. Sardenberg RA, Secaf LB, Pinotti AC, Taricco MA, Brock RS, Younes RN. Diaphragmatic pacing: unusual indication with successful application. [Article in English, Portuguese]. J Bras Pneumol 2011 Sep-Oct;37(5):697–9.

5. Chen ML, Tablizo MA, Kun S, Keens TG. Diaphragm pacers as a treatment for congenital central hypoventilation syndrome. Expert Rev Med Devices 2005 Sep;2(5):577–85.

6. Kun SS, McComb JG, Shaul DB, Atkinson JB, Keens TG. 23 years of diaphragmatic pacing in children. Am J Respir Crit Care Med 2004 Jul;172(2):200–5.

7. Straus C, Trang H, Becquemin MH, Touraine P, Similowski T. Chemosensitivity recovery in Ondine’s curse syndrome under treatment with desogestrel. Respir Physiol Neurobiol 2010 Apr 30;171(2):171–4.
Edorium Journals: An introduction

Edorium Journals Team

About Edorium Journals
Edorium Journals is a publisher of high-quality, open access, international scholarly journals covering subjects in basic sciences and clinical specialties and subspecialties.

Invitation for article submission
We sincerely invite you to submit your valuable research for publication to Edorium Journals.

But why should you publish with Edorium Journals?
In less than 10 words - we give you what no one does.

Vision of being the best
We have the vision of making our journals the best and the most authoritative journals in their respective specialties. We are working towards this goal every day of every week of every month of every year.

Exceptional services
We care for you, your work and your time. Our efficient, personalized and courteous services are a testimony to this.

Editorial Review
All manuscripts submitted to Edorium Journals undergo pre-processing review, first editorial review, peer review, second editorial review and finally third editorial review.

Peer Review
All manuscripts submitted to Edorium Journals undergo anonymous, double-blind, external peer review.

Early View version
Early View version of your manuscript will be published in the journal within 72 hours of final acceptance.

Manuscript status
From submission to publication of your article you will get regular updates (minimum six times) about status of your manuscripts directly in your email.

Our Commitment

Six weeks
You will get first decision on your manuscript within six weeks (42 days) of submission. If we fail to honor this by even one day, we will publish your manuscript free of charge.*

Four weeks
After we receive page proofs, your manuscript will be published in the journal within four weeks (31 days). If we fail to honor this by even one day, we will publish your manuscript free of charge and refund you the full article publication charges you paid for your manuscript.*

Favored Author program
One email is all it takes to become our favored author. You will not only get fee waivers but also get information and insights about scholarly publishing.

Institutional Membership program
Join our Institutional Memberships program and help scholars from your institute make their research accessible to all and save thousands of dollars in fees make their research accessible to all.

Our presence
We have some of the best designed publication formats. Our websites are very user friendly and enable you to do your work very easily with no hassle.

Something more...
We request you to have a look at our website to know more about us and our services.

* Terms and condition apply. Please see Edorium Journals website for more information.

We welcome you to interact with us, share with us, join us and of course publish with us.