Noninvasive ventilation via bilevel positive airway pressure improved sleep in a child with congenital central hypoventilation syndrome: a case report

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June 10, 2022

Abstract

Congenital central hypoventilation syndrome (CCHS) is rare in the world and the survival rate is low. The surviving children need lifelong ventilatory support. The sleep is closely related to nervous system development; however, there is a lack of studies on sleep in patients with CCHS.

Introduction

Congenital central hypoventilation syndrome (CCHS) is a rare condition with an incidence rate of 1/148000˜1/ 200000 live births[1]. It is characterized by the lack of adequate autonomic control of breathing. CCHS causes alveolar hypoventilation and reduced or absent ventilatory responses to hypercapnia and hypoxia, mainly during sleep. At the early stage of CCHS, most children only manifest abnormal ventilation during sleep. With the development of CCHS, alveolar hypopnea also occurs when the patients are awake during the day. Therefore, it is necessary to start the ventilatory support as early as possible and maintain it lifelong for patients with CCHS.

It is well known that ventilation of the children with CCHS can be successfully managed by non-invasive ventilation[2]. However, it is not clear whether the noninvasive ventilation can improve the sleep of children with CCHS. Sleep is closely related to nervous system development. This paper introduces a child with CCHS whose sleep was improved significantly by using effective bi-level positive airway pressure (BiPAP).

Case Presentation

A two-year-old girl presented to our hospital because she had 2 convulsions in the last 10 days. She was previously diagnosed with CCHS with genetic testing showing a mutation in exon 3 of Phox2b (genotype 20/25). She had been treated with BiPAP (PHILIPS BiPAP AVAPS 30) and oxygen inhalation (FiO_2: 30%) via a nasal oxygen cannula for a year before presenting to our hospital. Results of exams during sleep were as follows: saturation of oxygen (SpO_2): 80%; heart rate (HR):110 beats per min (bpm); and transcutaneous partial pressure of carbon dioxide ($TcpCO_2$): 88 mmHg. The BiPAP was set at S/T mode (Spontaneous Time) as follows: inspiratory positive airway pressure (IPAP):16 cmH_2O; expiratory positive airway pressure (EPAP): 4 cmH_2O; backup respiratory rate: 25 breaths/min; and inspiratory time: 0.8 s. The brain nuclear magnetic resonance showed no obvious abnormality. After the patient was admitted, we found her nasal oxygen cannula caused massive air leakage around the nasal area. We replaced her nasal oxygen cannula with a nasal mask. The parameters of ventilator were reset as follows: IPAP: 12 cmH_2O; EPAP: 5 cmH_2O, backup respiratory rate: 20 breaths/ min; and inspiratory time: 1.1s. Respiratory variables during sleep were improved significantly after 1 month of treatment. Under spontaneous breathing without oxygen inhalation, SpO_2 was above 95%, the average HR was 70-80 bpm, and $TcpCO_2$ was less than 50mmHg. During the

1-year follow-up, there were no convulsions observed. We monitored the patient's oxygen saturation remotely and instructed the parent to adjust the BiPAP according to the oxygen saturation. All her neurocognitive evaluations showed normal results.

Fig. 1 shows the polysomnographies during sleep under spontaneous breathing (with no oxygen inhalation) at admission (baseline), and 1 month and 1 year after the BiPAP treatment. As shown in Table 1, the percentage of rapid eye movement (REM) was 3.5% at the baseline; it was increased at 1 month (19.8%) and 1 year (12.5%) after the treatment. The baseline percentage of stage N3 was 96.5%, it was decreased to 53.8% and 28.8% at 1 month and 1 year, respectively. There was no stage N1 or stage N2 at the baseline. The percentage of stage N1 was increased at 1 year (2.4%). The stage N2 sleep was increased to 26.3% and 56.3% at 1 month and 1 year, respectively. The baseline average SpO_2 was 85%; it was improved to 91% and 93% at 1 month and 1 year, respectively. The oxygen desaturation index was 30.1 times/h at baseline; it was decreased to 21.1 and 11.3 times/h at 1 month and 1 year, respectively. The microarousals index was increased at 1 month (2.4 times/h) and 1 year (10.5 times/h) compared to the baseline (0.9 times/h).

Discussion

For this patient with CCHS, with effective treatment of BiPAP, the sleep structure, SpO_2, HR and the ability of arousal were improved significantly under spontaneous breathing.

For CCHS patients, maintaining successful ventilation is critical for respiratory management. Typically, there are two approaches to establish artificial airway for in patients with CCHS: tracheotomy and non-invasive ventilation. The non-invasive ventilation approaches included pressure-controlled BiPAP and volume-targeted BiPAP, both can adopt S/T mode. The BiPAP with S/T mode has been successfully applied to the children with CCHS when the tracheotomy was declined by their parents. For patients with CCHS, sometimes they are incapable to trigger the ventilator to switch from IPAP to EPAP during sleep due to the dysfunction of respiratory center. When set at the S/T mode, if spontaneous breathing does not occur within a certain period of time, the BiPAP will provide one mechanically triggered breathing according to the preset IPAP time. Therefore, the BiBAP S/T mode can help the patients with abnormal central ventilation control switch between IPAP and EPAP effectively.

Choosing a proper interface is important for the success of non-invasive ventilation. There are five major interfaces based on the way the pressured air is supplied: oronasal (full-faced) mask, nasal mask, nasal pillow, oral mask, and total face mask. Each interface has its advantages and disadvantages. One of the considerations in choosing a proper interface is to avoid the unintended air leakage. For this case, the BiPAP device did not function effectively because of the massive air leakage caused by the nasal cannula. Therefore, we replaced the nasal cannula with a nasal mask.

Supplemental oxygen is used to enhance oxygen saturation when noninvasive ventilation is not adequate. However, oxygen supplementation alone is insufficient to improve ventilation, since it does not correct the hypoventilation. Thus oxygen supplementation without correcting hypoventilation may result in chronic hypercapnia, leading to the development of cor pulmonale. Therefore, it is recommended that the pressure of BiPAP should be adjusted first before considering supplementing oxygen. For this child, although normal oxygen saturation could be achieved by oxygen supplementation, excess carbon dioxide could not be expelled through gas exchange. The sustained carbon dioxide retention might be the reason for repetitive convulsions. Prolonged tachycardia may lead to excessive load on the heart, which may lead to heart failure. After adjustment of parameters of BiPAP and replacement the nasal cannula with a nasal mask, the child did not have any convulsions; her heart rate decreased to the normal range.

CCHS mostly occurs during sleep. It has been shown that patients with CCHS have more severe hypoventilation and central apneas during non-rapid eye movement (NREM) sleep than REM sleep; this may be due to increased excitatory inputs to the respiratory system during REM sleep[3]. In addition, it has been shown that the patients with CCHS do not arouse in response to endogenous hypoxemia and hypercapnia if they only depend on their spontaneous breathing during sleep. Once they get well-ventilated during sleep, they will arouse in response to exogenous hypercapnia and hypoxia[4,5]. Guilleminault et al. reported that the

degree of arousal in patients with CCHS was depended on the level of end-tidal PCO_2 and sleep stage[6], indicating the ability of arousal in CCHS patients was affected by the efficiency of ventilation. For this case, the patient's arousal ability was increased significantly after effective noninvasive ventilation support.

Sleep stage, especially REM sleep, is closely related to the development of nervous system in children. REM sleep can help facilitate the formation and consolidation of certain types of memory. Under normal development, REM sleep accounts for up to 55% of the total sleep time in infancy. With the development and maturity of the brain, REM sleep gradually decreases until it reaches the level of adults (20 - 25%) at the age of 5[7]. REM sleep can be affected by the abnormal breathing during sleep. We previously reported that the children with decreased REM sleep (REM $<$ 10%) had severer apnea-hyponea index and more obvious behavioral problems.[8,9] It has been shown that patients with CCHS may suffer from a spectrum of neurocognitive impairment[10]. We found that the percentage of REM sleep was increased after effective BiPAP treatment from 3.5% to 10% or more. The patient had no significant impairment of neurocognition at the follow-up.

Conclusions

In this patient, with effective treatment of BiPAP using a nasal mask, the spontaneous breathing, sleep structures and arousal ability were improved.

Acknowledgement

Not applicable

Author's contributions

DL and LY participated in the design of study and drafting the manuscript. LY, SQ and JZ conceived of the study and helped to draft manuscript. All authors read and approved the final manuscript.

Funding

No funding was received for the paper.

Availability of data and materials

All data generated during this case report are included in this published article.

Declarations

Ethics approval and consent to participate

Not applicable for this study;

Consent for publication

Written informed consent was obstained from the patient's parents for publication of the case report.

Competing interests

The authors declare that they have no competing interests.

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Table 1. Physiological variables and sleep parameters at baseline, and 1 month and 1 year after BiPAP treatment

Note: BiPAP: bilevel positive airway pressure; TRT: total recording time; TST: total sleep time; RL: R stage latency sleep, onset to first epoch of Stage REM in min; REM: Rapid eye movement, stage R; N1: stage 1; N2: stage 2; N3: stage 3; SpO_2: oxygen saturation; ODI: oxygen desaturation index; HR: heart rate; bpm: beats per minute.

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