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Original Article

Central sleep apnea in children: experience at a single center

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ABSTRACT

Objective: Central sleep apnea (CSA) syndromes are rare in children and data in children over one year of age are scarce. The aim of the study was to describe the sleep characteristics, underlying disorders, management, and outcome of children with CSA.
Patients/Methods: A retrospective chart review of all children >1 year of age, diagnosed with CSA on a laboratory sleep study during a 20-month period, was performed. CSA was defined by a central apnea index (CAI) >5 events/h. The clinical management and the patient's outcome were analyzed.
Results: Eighteen of 441 (4.1%) patients recorded during the study period had CSA. The median CAI, pulse oximetry, and oxygen desaturation index were 13/h (range 6–146), 96% (93–98%), and 18/h (6–98), respectively. Neurosurgical pathologies represented the most common underlying disorders with Arnold–Chiari malformation in four and ganglioglioma in three patients. Other underlying disorders were Prader–Willi syndrome ($N = 3$), achondroplasia ($N = 2$), and Down syndrome, with one patient having an achondroplasia and a Down syndrome. The remaining six patients had other genetic diseases. The most common investigation was brain magnetic resonance imaging (MRI). Individualized management with neurosurgery and/or chemotherapy, continuous positive airway pressure (in two patients having associated obstructive events), or noninvasive ventilation resulted in an improvement in CSA and the clinical presentation in 11 patients.
Conclusion: CSA is rare in children >1 year of age. Underlying disorders are dominated by neurosurgical disorders. Individualized management is able to improve CSA and the clinical condition in most patients.

1. Introduction

Central sleep apnea (CSA) is a rare but serious condition that may be associated with arterial oxygen desaturation, increase in carbon dioxide, arousals, and a hyperadrenergic state [1]. CSA is defined as the absence of chest and abdominal movements associated with a cessation of airflow for more than 20 s, or lasting more than two baseline respiratory cycles if associated with an arousal, an awakening or an oxygen desaturation of at least 3% [2]. The central apnea index (CAI) is defined as the number of central apneas per hour of sleep. Central apneas (CAs) are physiological in newborns and infants, whose index of up to five events per hour is considered within the normal range [3,4]. Although a CAI >1/h is by convention diagnostic of CSA, a CAI up to 5/h has been reported in healthy children [4–8]. Therefore, a CAI >5/h is considered by some authors to be outside the normal range [9].

CSA is the hallmark of congenital central hypoventilation syndrome (CCHS), which is a rare genetic disease associated with a *PHOX2B* mutation [10]. CSA is rare outside of this situation and only limited data have been reported in the literature about children over one year of age. Most observations are case reports and few series on children have been reported [9]. Brainstem lesions, such as Arnold–Chiari malformation, or brainstem compression, as observed in patients with mucopolysaccharidosis or achondroplasia, may also be responsible for CSA [11–14]. CSA has also been observed in association with Prader–Willi syndrome and hypothyroidism [15–17].

The aim of the study was to describe the sleep characteristics, underlying disorders, management, and outcome of children over one year of age diagnosed with CSA at a single pediatric sleep center.

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2. Methods

2.1. Patients

All the patients between the ages of one and 18 years who underwent an overnight level 3 polysomnography (PSG) or polygraphy (PG) in our sleep laboratory between September 2013 and April 2015 were considered for inclusion. Patients were referred to the sleep laboratory either for symptoms of sleep-disordered breathing or because of an underlying disease that is associated with an increased risk of sleep-disordered breathing. Only patients with a CAI >5/h were identified for further analysis. Patients with CCHS were excluded. The medical records of all the patients were systematically reviewed and data were collected on the patient's medical history and demographics. Interventions after the baseline sleep study, subsequent sleep studies, and outcomes were analyzed for every patient. The study was conducted in agreement with the French regulations and received appropriate legal and ethical approval from the Ethical Committee of Necker University Hospital (CPP Ile de France II).

2.2. Overnight sleep studies

All sleep studies were performed in the sleep laboratory of Necker hospital. All patients were accompanied by one parent throughout the night. Neither sedation nor sleep deprivation was used on any patient.

The following standardized measurements were simultaneously recorded during every level 3 PSG or PG: nasal flow through a nasal pressure transducer, pulse oximetry by a pulse oximeter (SpO_2), oximeter pulse wave form, thoracic and abdominal respiratory inductance plethysmography, digital synchronized infrared video monitoring (Cidelec, St Gemmes sur Loire, France or Alice 6, Philips Respironics, St Priest, France), and transcutaneous carbon dioxide pressure ($PtcCO_2$, SenTec, Therwil, Switzerland). For PSG, the following data were also recorded: electroencephalogram (C_3A_2, C_4A_1, O_1A_2, and O_2A_1), right and left electro-oculogram, submental, anterior tibialis electromyogram, and electrocardiography.

Scoring of sleep stages and respiratory events were performed according to the actualized 2012 scoring rules of the American Academy of Sleep Medicine [2]. The following definitions for respiratory events were used for scoring purposes [2]. CA was defined as the absence of airflow with the cessation of respiratory effort, lasting more than 20 s or of shorter duration and associated with an arousal and/or a 3% oxygen desaturation. CA occurring after gross body movements or after sighs was not included in the analysis. Obstructive apnea (OA) was defined as the absence of nasal airflow with continued chest wall and abdominal movements for at least two breaths. Mixed apnea was defined as an apnea that usually begins as central and ends as obstructive according to changes in the chest, abdominal, and flow traces. Hypopnea was defined as a decrease in nasal airflow of at least 30% with a corresponding decrease in pulse oximetry (SpO_2) of at least 3% and/or an arousal. The apnea–hypopnea index (AHI) was calculated as the sum of apneas and hypopneas per hour of total sleep time. An obstructive AHI (OAHI) <1.5/h and CAI <5/h were considered as normal. All the PSGs/PGs were scored by two experienced pediatric sleep specialists.

Mean, minimal SpO_2 values, and the percentage of total sleep time spent with SpO_2 <90% were calculated. The oxygen desaturation index (ODI) was defined as the number of SpO_2 drops of at least 3% per hour of total sleep time. Mean, maximal values of $PtcCO_2$ and the percentage of total sleep time spent with a $PtcCO_2$ >50 mmHg were calculated.

Repeat sleep studies were performed or planned for all 18 patients. As there are no recommendations or guidelines, we chose to define an improvement by a >50% reduction in the CAI in the repeat sleep studies as it was thought to represent a true change rather than intra-individual variability.

3. Results

3.1. Patients

Four-hundred and forty-one children over the age of one year underwent an overnight sleep study in our laboratory during the study period. Eighteen patients (4.1%) had a CAI >5/h (Table 1).

Apneas during sleep and wakefulness were reported only by the parents of patient #7 who suffered from a ganglioglioma; all the other patients had no symptoms of sleep-disordered breathing and were referred to the sleep laboratory for a systematic sleep study.

Neurosurgical pathologies represented the most common underlying disorders with four patients (patients #1 to #4) having an Arnold–Chiari malformation and three patients (patients #5 to #7) having a ganglioglioma. Other underlying disorders were Prader–Willi syndrome ($N = 3$, patients #8 to #10), achondroplasia ($N = 2$, patients #11 and #12), and Down syndrome (patient #13), with patient #12 having both an achondroplasia and a Down syndrome. The remaining five patients had various other genetic diseases (patients #14 to #18).

3.2. Polygraphic data

A level 3 PSG was performed in two patients (patients #6 and #10) whereas a PG was performed in all the other patients. The CAI was highly variable with five patients having a CAI between 5/h and 6/h (patients #3, #4, #13, #16, and #17), the other patients having a CAI between 11/h and 146/h, with the highest value being observed in a patient with a ganglioglioma (patient #5). Four patients had exclusively CSA (patient #2 and patients #16 to #18) whereas two other patients (patients #13 and #15) also had some obstructive events. Mean SpO_2 was ≥94% in all the patients except in patient #2 who had an Arnold–Chiari malformation. Minimal SpO_2 was below 90% except in one patient with Prader–Willi syndrome (patient #2) but only two patients spent more than 1% of the recording time with a SpO_2 <90% (patients #1 and #13). The ODI was very high with a median value of 18/h. Only two patients had a maximal $PtcCO_2$ >50 mmHg (patients #7 and #13).

3.3. Interventions and outcome of the patients

Table 2 shows intervention and outcome of the patients.

A brain magnetic resonance imaging (MRI) was performed in all the patients. This MRI revealed a cervico-medullary compression in six patients, in the four patients with an Arnold–Chiari malformation, in one patient with a ganglioglioma (patient #7), and another patient with achondroplasia (patient #12). A cervico-medullary decompression was performed in five patients (patients #1, #2, #3, #4, and #7) and could not be performed in patient #12 (achondroplasia with Down syndrome). Patient #1 was successfully managed by noninvasive ventilation (NIV) due to persistence of the CSA after the cervico-medullary decompression. Patient #3 required a tracheostomy after the cervico-medullary decompression because of an increase in CSA. A modification of the chemotherapy was associated with an improvement in CSA in patient #6 who suffered from a ganglioglioma. The other patient with a ganglioglioma (patient #7) was successfully managed with servo-assisted ventilation after the persistence of CSA despite a cervicomedullary decompression. A spontaneous resolution of the CSA was observed in one patient with Prader–Willi syndrome (patient #9) and one patient with achondroplasia (patient #11). Acetazolamide was tried in the two patients with Prader–Willi syndrome (patients #8 and #10). A 50% reduction in CAI was