Sleep Hypoventilation Syndromes and Noninvasive Ventilation in Children

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KEYWORDS

• Hypoventilation • Children • Nocturnal noninvasive ventilation • Bilevel positive airway pressure

KEY POINTS

- Current evidence supports the application of noninvasive ventilation devices in most disorders of nocturnal hypoventilation in childhood.
- Technical limitations inherent to noninvasive ventilation devices must be acknowledged before using these devices in children.
- Current evidence supports bilevel positive airway pressure devices in treating childhood nocturnal hypoventilation disorders. Novel devices already established in treating adults with sleep-disordered breathing may represent alternative strategies in treating young children.
- Studies have revealed favorable outcomes regarding adherence to these devices in children.

The wide spectrum of nocturnal hypoventilation in children is attributable largely to the various disturbances of normal ventilation related to a plethora of disease states that can affect either the central ventilatory drive or the ventilatory mechanical apparatus. Our understanding of diseases that lead to hypoventilation during childhood has evolved a great deal over the years. In parallel, any discussion of supportive ventilation including noninvasive ventilation in children would reveal a progression of clinical practice over the past several decades. Classically, invasive mechanical ventilation, typically via a tracheostomy, was the mainstay in managing many disorders of hypoventilation in children, ranging from infectious destruction of anterior horn cells, as is the case in poliomyelitis, to gene-specific disorders such as congenital central hypoventilation syndrome. However, with advances in noninvasive ventilation in adults its implementation in children was also initiated, but has only recently emerged as an efficacious treatment of disordered breathing in young persons. Furthermore, in the context of conditions under which supportive ventilation is only required at night, whereby the need for a permanent interface such as a tracheostomy can be obviated altogether, the application of noninvasive ventilation becomes highly attractive.

Before a discussion of nocturnal noninvasive ventilation (nNIV) in children, one must acknowledge that clinicians' familiarity with its use stems from the vast experience of these devices in adults with sleep-disordered breathing (SDB). Notwithstanding, the evidence, particularly from studies with large sample sizes, supporting its use in managing SDB in children is sparse. In fact, despite the

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Sleep Med Clin 9 (2014) 441–453
http://dx.doi.org/10.1016/j.jsmc.2014.05.009
1556-407X/14/$ – see front matter

evidence from published studies, nNIV remains to be approved by the Food and Drug Administration (FDA) for use in children weighing less than 30 kg.

In discussing nNIV in treating children with nocturnal hypoventilation disorders, a brief introduction to the pathophysiology of hypoventilation in children is relevant. As hypoventilation disorders in children are discussed elsewhere in this issue by Weese-Meyer and colleagues, herein each of the major categories and conditions of hypoventilation disorders is addressed, including insight into their prevalence and the challenges to diagnosis. The efficacy of current treatment strategies is discussed, including the indications for noninvasive ventilation in children and an analysis of the evidence that describes the unique hurdles that are emerging in the context of adherence among children using noninvasive ventilation. Lastly, evidence is presented suggesting novel modalities that have become recently available and may be applied to children in an off-label manner.

It is crucial to bear in mind that delineation of the specific indications for implementation of nNIV in children has yet to be defined in a formal consensus statement, and there is clearly a pressing need for such guidelines, as illustrated by the beneficial outcomes regarding life expectancy in children and adults with specific hypoventilation syndromes.[1,2]

NOCTURNAL ALVEOLAR HYPOVENTILATION IN CHILDREN

A heterogeneous group of conditions can culminate in nocturnal alveolar hypoventilation in children of variable severity (**Box 1**). Salient conditions include the classic congenital central hypoventilation syndrome (CCHS) but also encompass neuromuscular disorders, metabolic storage diseases including obesity, and musculoskeletal confinement of the thoracic cage, as in the case of scoliosis or thoracic dystrophies. The marked variance in antecedents of nocturnal alveolar hypoventilation is the central hurdle to establishing universal practice parameters for the care of these children, as the progression of disease and overall prognosis differs drastically.

As outlined by *The International Classification of Sleep Disorders* (second edition) (ICSD-2),[3] nocturnal alveolar hypoventilation consists of reduced ventilation secondary to decreased tidal volume, with ensuing hypercapnia and/or hypoxemia. As a manifestation to this variant of sleep-disturbed breathing, there often is accompanying sleep fragmentation related to increases in lighter sleep stage, transient arousals, and/or awakenings. The muscular atonia, a feature of rapid eye movement (REM) sleep, augments this variant of SDB in most disease states associated with nocturnal hypoventilation with the exception of CCHS, in which non-REM (NREM) stage III sleep accounts for more profound changes in ventilation.

The normative alveolar ventilatory parameters of children during sleep have been only recently defined. In a cross-sectional study of 542 children undergoing nocturnal polysomnography by Montgomery-Downs and colleagues,[4] average nocturnal oxygen saturations, oxygen saturation nadir, and oxygen desaturation indices did not differ by age. Furthermore, end-tidal carbon dioxide ($ETco_2$) measurements captured by nocturnal polysomnography did not differ by age, with the average $ETco_2$ being 40.7 mm Hg. Twenty percent of studied children spent 50% or more of total sleep time with an $ETco_2$ of at least 45 mm Hg, and 2.2% spent 50% or more of total sleep time with an $ETco_2$ of at least 50 mm Hg. These findings closely concur with previous smaller-sized studies assessing normative polysomnographic measures in children.[5–7]

The ICSD-2[3] establishes criteria for nocturnal hypoventilation largely based on oxygen saturation (Spo_2) during polysomnography, such that hypoventilation is defined by an Spo_2 during sleep of less than 90% for more than 5 minutes, with a nadir of at least 85% or more than 30% of total sleep time at an of Spo_2 of less than 90%. A sleeping arterial blood gas level with a partial pressure of co_2 (Pco_2) that is abnormally high or disproportionately higher than during wakefulness can also define nocturnal hypoventilation. The diagnostic criteria for children are exclusively defined by carbon dioxide monitoring measured during polysomnography. Specifically, the American Academy of Sleep Medicine scoring manual[8] defines alveolar hypoventilation during sleep as greater than 25% of total sleep time spent with a Pco_2 greater than 50 mm Hg when measured by either the arterial Pco_2 or surrogate. Children, with an overall reduced pulmonary functional residual capacity (FRC), are especially prone to alveolar hypoventilation, which is the premise for routine monitoring of carbon dioxide during pediatric polysomnography.[8]

Although the aforementioned diagnostic criteria for alveolar hypoventilation need to be endorsed by a formal consensus process, there is great variance in opinion regarding the parameters for establishing nNIV in treating disorders associated with nocturnal hypoventilation in children. Recently, a task force put forth guidelines[9] for the treatment of hypoventilation syndromes in adults and children, and largely focused on the