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CASE REPORTS

Chewing gum: alternative therapy to oxygen intolerance

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Rapid-onset obesity with hypothalamic dysregulation, hypoventilation, and autonomic dysregulation (ROHHAD) syndrome is a rare complex disorder associated with alterations in the endocrine system, autonomic nervous system, and respiratory system. Previously published case reports and studies have noted sleep-disordered breathing in patients with ROHHAD syndrome. Nocturnal respiratory manifestations, which if untreated early by respiratory support, may cause cardiorespiratory arrest and a life-threatening condition. More recently, it has been recognized that children with ROHHAD syndrome have central pauses during wakefulness associated with intermittent oxygen desaturations. We report novel findings of a child with ROHHAD syndrome displaying an irregular breathing pattern and significant central pauses associated with oxygen desaturations during wakefulness, whose respiratory status improved while chewing gum. This was used as an alternative to supplemental oxygen therapy.

Keywords: chewing gum, mastication, ROHHAD, sleep-disordered breathing, children

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INTRODUCTION

Rapid-onset obesity with hypothalamic dysregulation, hypoventilation, and autonomic dysregulation (ROHHAD) syndrome is a rare disorder in childhood.[1,2] Children with ROHHAD syndrome can have significant and variable nocturnal and daytime respiratory compromise requiring long-term ventilatory support.[2,3]

REPORT OF CASE

A 10-year-old male, with no significant past medical history or underlying symptoms of pulmonary disease including asthma, presented with rapid weight gain, increasing fatigue, excessive daytime somnolence, and snoring. On initial evaluation, he was noted to be adipsic with sodium of 178 mmol/L, potassium of 3.4 mmol/L, and creatinine of 108 μmol/L. He was slowly rehydrated with normalization of sodium and creatinine. His symptoms improved and brain/spine magnetic resonance imaging as well as abdominal and renal ultrasound doppler imaging were normal at this time. He underwent a baseline polysomnography, which showed severe obstructive sleep apnea (OSA; obstructive apnea-hypopnea index [OAHI] of 49.3 events/h) and mild central sleep apnea (central apnea-hypopnea index [CAHI] of 6.9 events/h). His baseline oxygen saturation (SaO_2) was 97%, with a nadir SaO_2 of 82% and an average transcutaneous carbon dioxide ($tcCO_2$) of 38 mmHg.

He subsequently underwent an adenotonsillectomy 4 months later. However, 3 months post-adenotonsillectomy, he presented to his local hospital with reduced levels of consciousness, prolonged oxygen desaturation (baseline SaO_2 93% and nadir SaO_2 65%), and hypercapnia (partial pressure of CO_2 [pCO_2] 82 mmHg), as well as observed central pauses while awake. He was also noted to have bradycardia (mean heart rate of 33 beats/minute), temperature instability (average temperature 33°C), central hypothyroidism, and hyperprolactinemia. All signs and symptoms were compatible with ROHHAD syndrome, which was his working clinical diagnosis. Further investigations including electroencephalogram, whole-body magnetic resonance imaging, and echocardiogram, were unremarkable. He was negative for *PHOX2B* gene mutations. Repeat polysomnography (7 months after the first polysomnography) demonstrated severe OSA (OAHI > 100 events/h), central sleep apnea (CAHI of 12 events/h) with nadir SaO_2 of 46%, hypercapnia (maximum of $tcCO_2$ was 55 mmHg), and an irregular breathing pattern of 6–10 breaths/minute characterized by slow respiratory rates alternating with pauses; therefore, bilevel positive airway pressure was recommended for nocturnal sleep.

He also underwent daytime cardiopulmonary monitoring while awake with full polysomnography set up to evaluate his daytime cardiopulmonary parameters and gas exchange. His daytime monitoring involved him sitting upright in a chair and participating in quiet activities including reading books, watching television, and eating. During his daytime monitoring, it was noted that he had central pauses defined by the absence of respiratory effort related to airflow cessation with an associated 3% or greater oxygen desaturation while awake, and an irregular breathing pattern (shallow breathing interspersed with normal tidal breathing), with an average respiratory rate of 6–10 breaths/minute associated with significant oxygen desaturations (nadir

SaO_2 81%). Moreover, there were no abnormalities in his electroencephalogram and no evidence of hypercapnia (see **Table 1**). Supplemental oxygen was trialed while awake, which improved oxygen desaturations with no evidence of hypercapnia.

During nocturnal sleep, he was treated with bilevel positive airway pressure, which controlled his sleep-disordered breathing. He was also prescribed oxygen for daytime use. Although he was adherent to his nocturnal bilevel positive airway pressure, he refused to wear oxygen during the day as he did not like using it at school. On his repeat daytime cardiopulmonary monitoring and video recordings, we had incidentally observed that chewing improved his daytime awake oxygen saturations. Subsequently, he underwent formal daytime monitoring for 4.5 hours with the split time of chewing and not chewing gum (see **Table 1**). He took a formal trial of chewing gum with a chewing rate of 60–70/minute intermittently during simultaneous daytime monitoring. Interestingly, chewing gum was correlated with a pattern of respiratory improvement, which was observed during the duration that he chewed. **Figure 1** demonstrates a snapshot of a 60-second epoch of daytime cardiopulmonary monitoring comparing activity while chewing gum and not chewing gum. As observed in **Figure 1B**, chewing gum improved his irregular respiratory rate, decreased the frequency of central pauses, and improved his oxygen saturations. He was subsequently asked to chew gum intermittently during the day as frequently as possible. He did not report negative outcomes such as jaw pain or headaches while chewing gum.

DISCUSSION

ROHHAD is a rare disorder with high mortality rates.[1–3] The etiology of ROHHAD remains unclear, although it is believed to be a neuroinflammatory condition targeting the hypothalamus.[4] To date, there is no known diagnostic genetic test for ROHHAD and its diagnosis is dependent on clinical criteria including abnormal control of breathing. Our case patient was noted to have intermittent oxygen desaturations, central pauses, and irregularly low respiratory rates, which responded to a trial of chewing gum. In our case, chewing gum increased his respiratory rate and improved his oxygen saturations.

Breathing is a complex mechanism requiring coordination between neurological drive and respiratory muscle as well as upper airway muscle.[5–7] In mammals, there are many nuclei associated with respiration and feeding (such as chewing, swallowing, and sucking) in the pons of the brainstem, which coordinate and integrate harmoniously.[8,9] Fontana and colleagues[6] studied and demonstrated that mastication during the chewing of gum resulted in an increase in respiratory rate in 9 healthy volunteers. This increase in respiratory rate results in an overall increase in minute ventilation.[6] Mastication also triggers the peripheral neurogenic factors connected to the dorsal respiratory group, which plays a major role in breathing pattern control.[6,10] Thus, mastication can promote a beneficial ventilatory response through the complex interactions between respiratory and nonrespiratory functions of the upper airway and chest wall muscles.[6]

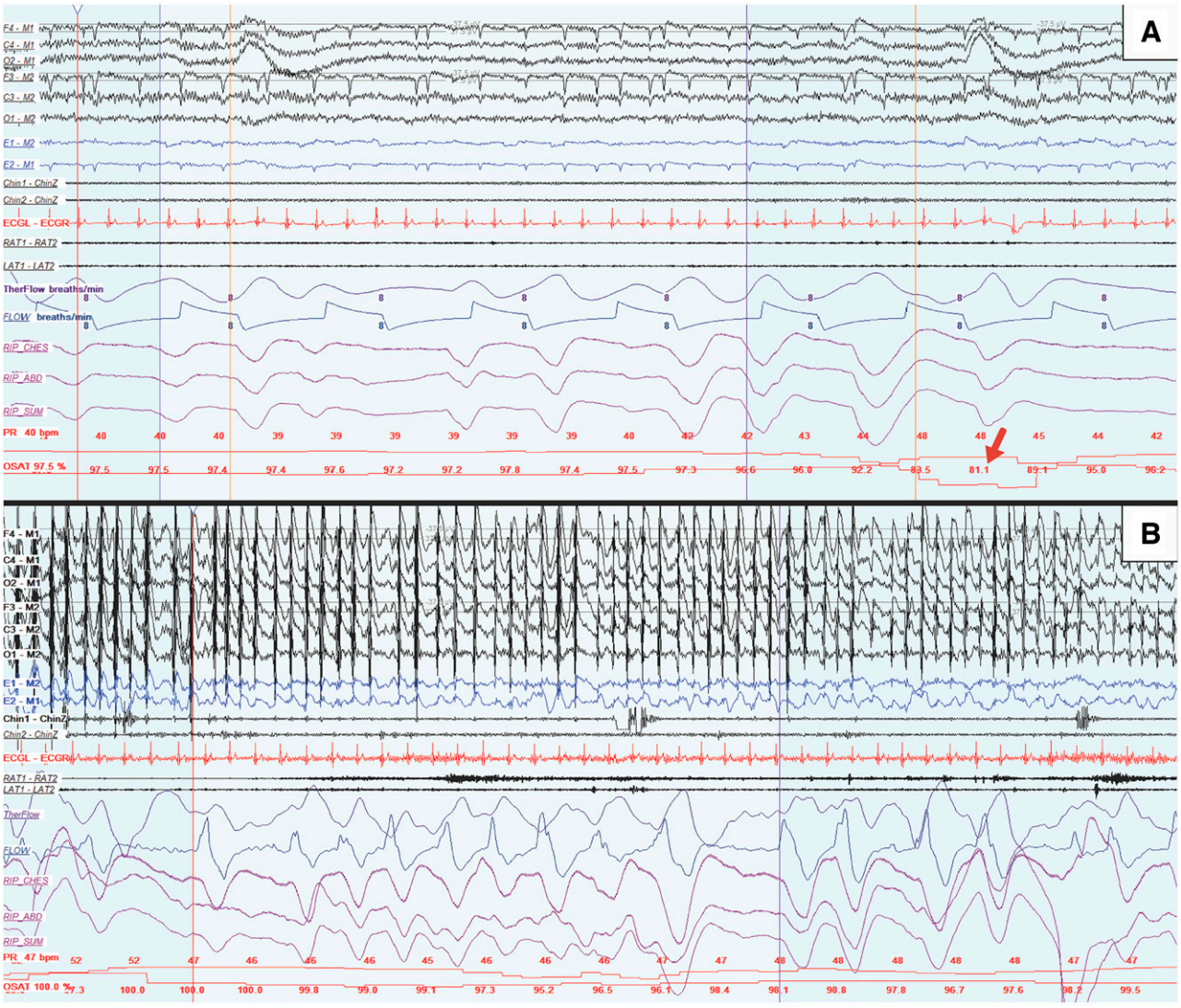
In summary, our case highlights the benefits of mastication with chewing gum that may be an alternative option for improving abnormal respiratory pattern and oxygen desaturations during daytime in children with ROHHAD syndrome. Although there was overall improvement, particularly in respiratory rate during chewing gum, there were persistent central pauses and oxygen desaturations. Of importance, chewing gum was the preferred therapeutic option to supplemental oxygen for our patient as he clearly articulated that he did not want to be

Table 1—Comparison of daytime cardiopulmonary monitoring parameters between not chewing gum and while chewing gum.

Parameters	Daytime Cardiopulmonary Monitoring	
	Not Chewing Gum	While Chewing Gum
Total time monitoring (min)	186	85.5
Central pauses (events)	82	24
Central pause index (events/h)	26.5	16.8
Desaturation index (events/h)	27.4	17.5
Average oxygen saturation (%)	97	98
Nadir oxygen saturation (%)	81	88
Average $tcCO_2$ (mmHg)	33	33
$tcCO_2$ range (mmHg)	31–43	31–42
Average respiratory rate (/min)	8	12
Respiratory rate range (/min)	6–10	12–16
Average heart rate (/min)	44	46
Heart rate range (/min)	40–72	42–78

$tcCO_2$ = transcutaneous carbon dioxide.

Figure 1—Sixty-second epoch of daytime cardiopulmonary monitoring using a polysomnography set up.



(A) Lower respiratory rate with pulses in breathing and associated oxygen desaturation (nadir SaO_2 was 81%). **(B)** Respiratory rate and oxygen desaturations improved while chewing gum.

medicalized in his school environment and would thus not use supplemental oxygen at school.

ABBREVIATIONS

ROHHAD, rapid-onset obesity with hypothalamic dysregulation, hypoventilation, and autonomic dysregulation
SaO_2, oxygen saturation
$tcCO_2$, transcutaneous carbon dioxide

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DISCLOSURE STATEMENT

All authors have seen and approved the final manuscript. The legal guardians or the parents have consented to the submission of the data to the journal. The authors report no conflicts of interest.