ELSEVIER

Sleep Medicine 3 (2002) 179–180

SLEEP MEDICINE

www.elsevier.com/locate/sleep

Journal search and commentary

Article reviewed: Sleep-disordered breathing and respiratory failure in acid maltase deficiency ☆

Alex Iranzo*

Neurology Service, Hospital Clinic i Provincial de Barcelona, C/Villarroel, 08036 Barcelona, Spain

Accepted 4 January 2002

Objectives

To study the incidence, clinical significance and relationship between wake respiratory dysfunction and sleep-disordered breathing in patients with acid maltase deficiency (AMD).

Study design

A cross-sectional description and analysis of the waking and sleep respiratory dysfunction of a group of patients with AMD.

Study population

Twenty-seven patients with biochemically confirmed AMD, seven with the juvenile type (mean age, 12.4 ± 9.5 years) and 20 with the adult type (mean age, 46.7 ± 12.1 years). Nine patients (33%) were non-ambulatory. Thirteen subjects (three juvenile, ten adult) had symptomatic dyspnea during wakefulness, and seven (two juvenile, five adult) required ventilatory support.

Methods

Respiratory lung and diaphragm function during wakefulness were assessed using arterial blood gases and both erect and supine spirometry (inspiratory vital capacity, forced vital capacity, peak inspiratory muscle pressure). Ventilatory restriction was defined as an inspiratory vital capacity <80%, and diaphragm weakness as a postural drop >20%. Respiratory function during sleep was studied by standard polysomnography with oxyhemoglobin saturation and transcutaneous PCO_2 measurement. Sleep-disordered breathing was defined as an apnea-hypopnea index >10, and nocturnal hypoventilation as an oxyhemoglobin saturation <90% plus a transcutaneous PCO_2 >50 mmHg.

Results

Ventilatory restriction occurred in 17 subjects (63%). Inspiratory vital capacity was significantly associated with lower peak inspiratory muscle pressure, daytime gas exchange impairment, nocturnal hypoventilation and higher functional disability. Diaphragm weakness was present in 13 patients (48%) and was related to longer disease course and gas exchange impairment. Sleep-disordered breathing was detected in 13 subjects (48%), 11 with diaphragm weakness, and was predicted by diaphragm weakness and inspiratory vital capacity. Respiratory events were mainly hypopneas, occurred first and more frequently during REM sleep than during non-REM sleep, and were associated with hypoventilation.

Conclusions

In patients with AMD both restrictive pulmonary dysfunction and sleep-disordered breathing, characterized by hypoventilation and REM sleep related hypopneas, frequently occur and are secondary to diaphragm weakness. Severity of daytime diaphragm weakness and inspiratory vital capacity predict the presence of sleep-disordered breathing.

Comment

This article groups together 27 patients with the juvenile and adult forms of AMD, which may be considered a representative sample for a study of this rare myopathy. The

☆ Mellies U, Ragette R, Schwake C, Baethmann M, Voit T, Teschler H. Neurology 2001;57:1290–1295.

* Tel.: +34-93-227-5413; fax: +34-3227-5454.

PII: S1389-9457(02)00021-7

authors studied the patients both during sleep and wakefulness, allowing evaluation of possible association between the respiratory parameters of these two states in this metabolic myopathy. In addition, the article provides the opportunity to compare AMD with other neuromuscular disorders such as amyotrophic lateral sclerosis and Duchenne's muscular dystrophy where also: (a) diaphragm weakness and ventilatory dysfunction are frequent findings that influence the course and prognosis of the disease; (b) the most common cause of death is respiratory failure; and (c) some patients have died unexpectedly during sleep [1].

The results found in this article support the idea that neuromuscular disorders associated with severe involvement of the diaphragm, relative sparing of the upper airway muscles, and no alterations in the brainstem respiratory centers, heart function and pulmonary parenchyma are associated with both frequent restrictive pulmonary dysfunction, characterized by reduction in lung volumes, and frequent sleep-disordered breathing, characterized by nocturnal hypoventilation, REM sleep hypopneas, and almost total absence of obstructive apneic events. In amyotrophic lateral sclerosis, a motor neuron disease in which diaphragmatic and pharyngeal musculature function may be equally affected, central and obstructive apneas coexist [2]. In contrast, in Charcot-Marie-Tooth disease, a neuropathy with rare involvement of the phrenic nerve and no primary lung dysfunction, sleep-disordered breathing is mainly characterized by obstructive apneic events related to pharyngeal neuropathy [3].

The finding that the respiratory events for AMD were first and commonly seen during REM sleep rather than during non-REM sleep, as is also observed in amyotrophic lateral sclerosis and Duchenne's muscular dystrophy, suggests prominent impairment of the diaphragm as the common causal factor; the physiologic REM-sleep-related muscle atonia causes an important reduction of the respiratory accessory muscles that would normally compensate for diaphragmatic weakness during REM and non-REM sleep.

One of the main findings of this study is that a coexisting decrease in amount of daytime ventilatory capacity and degree of diaphragmatic weakness are necessary to predict nocturnal hypoventilation and hypopneas. Previous evaluations in other neuromuscular disorders such as Myasthenia gravis, Myotonic dystrophy, Duchenne's muscular dystrophy and amyotrophic lateral sclerosis, did not find pulmonary function tests to be associated with the apnea-hypopnea index [4]. From these data, one might conclude that sleep studies must be performed in patients with AMD plus spirometry-detected pulmonary restrictive dysfunction in order to exclude sleep-disordered breathing, which may be treated, as was done in this study, with nocturnal non-invasive positive pressure ventilation. Moreover, given the high prevalence of sleep-disordered breathing in this sample it would seem prudent to include a clinical polysomnogram evaluation for sleep-disordered breathing as a routine part of the evaluation of these patients, regardless of their waking pulmonary status. Treatment of the SDB is likely to prevent or reduce some of the complications of this disorder.

Since most of the AMD patients studied in this article had daytime pulmonary dysfunction, it is very difficult to determine whether sleep-disordered breathing may precede daytime dysfunction in this disease, a finding that has been observed in other myopathies such as Duchenne's muscular dystrophy [5]. It is surprising that this well conducted sleep study did not mention whether the polysomnographic recordings showed cardiac arrhythmias during sleep and did not evaluate the occurrence of subjective sleep complaints such as daytime sleepiness or difficulty with sleep initiation and maintenance. Bradytachycardia during REM sleep, daytime sleepiness and sudden death during sleep have been reported in patients with AMD [1,6]. These disturbances also occur in myotonic dystrophy, but their pathogenesis may differ from AMD since they are related to brainstem and heart conduction abnormalities, which are not prominent in the adult and juvenile forms of AMD.

References

[1] Adams RD, Victor M. The metabolic myopathies. In: Adams RD, Victor M, editors. Principles of Neurology, 5th ed.. New York: McGraw-Hill, Inc, 1993. pp. 1233–1240.

[2] David WS, Bundlie SR, Mahdavi Z. Polysomnographic studies in amyotrophic lateral sclerosis. J Neurol Sci 1997;152(Suppl. 1):29–35.

[3] Dematteis M, Pépin JL, Jeanmart M, Deschaux C, Labarre-Vila A, Lévy P. Charcot-Marie-Tooth disease and sleep apnoea syndrome: a family study. Lancet 2001;357:267–272.

[4] Labanowski M, Schmidt-Nowara W, Guilleminault C. Sleep and neuromuscular disease: frequency of sleep-disordered breathing in a neuromuscular disease clinic population. Neurology 1996;47:1173–1180.

[5] Smith PE, Calverly PM, Edwards RH. Hypoxemia during sleep in Duchenne muscular dystrophy. Am Rev Respir Dis 1988;137:884–888.

[6] Guilleminault C, Stoohs R, Quera-Salva MA. Sleep-related obstructive and non-obstructive apneas and neurologic disorders. Neurology 1992;42(Suppl. 6):53–60.