



## And the Patient Said: “Let Me Be Able to Breathe and Dream”

Commentary on Vrijsen et al. Noninvasive ventilation improves sleep in amyotrophic lateral sclerosis: a prospective polysomnographic study. *J Clin Sleep Med* 2015;11:559–566.

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by progressive neuromuscular atrophy with early involvement of respiratory system, rapidly leading to alveolar hypoventilation, with consequent severe respiratory failure.

Noninvasive ventilation (NIV) has been indicated and recommended in ALS patients, since not only improves persistent hypoventilation, but may also extend life of individuals affected by this devastating disease. Specific guidelines have been proposed in order to monitor respiratory function and to properly start NIV.<sup>1,2</sup> A historical prospective controlled study found significantly increased survival in patients treated with NIV as compared to those receiving standard care.<sup>3</sup> More recently, a randomized controlled trial showed improved survival and quality of life (QoL) in ALS patients admitted to NIV when orthopnea occurred, associated with reduction of maximal inspiratory pressure < 60% of the predicted, except those with severe bulbar impairment.<sup>4</sup> Generally, the presence of sleep disturbances in ALS patients is attributed to respiratory impairment. Diaphragmatic impairment and/or respiratory muscle weakness is generally associated to a reduction in REM sleep amount or fragmentation, as well as reduced sleep efficiency.<sup>5</sup> An improvement in sleep quality and stability could be expected with the onset of mechanical ventilation. Indeed, the available clinical guidelines for ALS management suggested the NIV should be offered initially during the night.<sup>1,2,6</sup> Using it in this manner, NIV may reduce signs or symptoms of chronic alveolar hypoventilation. However, few studies explored the impact of NIV on sleep, and those show discordant results. Atkeson et al. observed in nineteen patients, treated with nocturnal NIV, frequent patient-ventilator asynchronies not predicted by demographic, functional severity or ventilatory settings.<sup>7</sup> They concluded that the use of NIV is unlikely to provide an optimal nocturnal ventilatory support. More recently, Katzeberg et al. observed that NIV is able to improve nocturnal gas exchange and ventilation without any effect on sleep structure or stability.<sup>8</sup>

The paper of Vrijsen et al.<sup>9</sup> presented in the current issue of *JCSM* gives us the opportunity to approach this problem in a different way and to obtain better clinical results. Usually, in clinical practice, physicians working in the field of chronic respiratory failure provide mechanical ventilation

during daytime according to patient's comfort, improvement in breathing pattern and changes in blood gases; the efficacy of NIV in reducing alveolar hypoventilation during sleep is often evaluated by nocturnal pulse oximetry or capnography. Authors of the current study used a different approach: they started the ventilatory titration during an afternoon nap to reach a tidal volume of 6 mL/min/kg of ideal body weight. Patients underwent to PSG for three consecutive nights: in the morning, they revised the PSG data and were able to modify the ventilatory setting (a sort of fine tuning) according to the picture observed during the night. In this way, they were able to measure a significant and stepwise improvement of nocturnal hypoventilation and improvement of sleep quality, both at the end of titration procedure and after 1-month follow-up. Similarly, they found an enhancement in QoL, daytime sleepiness and subjective sleep quality. All these improvement were evident in patients without bulbar impairment. On the contrary, they found in the bulbar patients a statistically significant increase of sleep oxygenation indices. Thus, in order to explain the lack of improvement, as a possible hypothesis the authors proposed that bulbar patients have less room to enhance sleep quality. Indeed at enrollment, bulbar patients showed better sleep quality and a better sleep alveolar ventilation.

This paper give us two messages: first, more studies are needed to identify the right time to start mechanical ventilation in bulbar patients; second, mechanical ventilation setting should be defined in a more physiological way and sleep recording should be required to properly assess the efficacy of NIV.

Can the model proposed by Vrijsen and colleagues be spread worldwide and became a possible “reference model” for titration of NIV in ALS patients? It is hard to answer.

The clinical best practices proposed by AASM stated that NPPV titration with PSG is the recommended method to determine an effective level of nocturnal ventilatory support in patients with chronic alveolar hypoventilation. Whether NPPV treatment is initiated and adjusted empirically, a PSG should be utilized if possible to confirm that the final NPPV settings are effective or to make adjustments as necessary.<sup>10</sup> On the contrary, Canadian guidelines indicated that ventilator setting should be adjusted for optimal patient comfort and improvement of symptoms; blood gas analysis and/ or nocturnal

oximetry and/or polysomnography are not required, but may be helpful in some circumstances.<sup>11</sup> Unfortunately, an alternative method, a split night protocol, was recently demonstrated to be unsuccessful.<sup>12</sup> A specific physiological protocol that include nocturnal oximetry or capnography or complete/partial sleep study, in the management of NIV in ALS patients may not be reliably performed in many Services or Hospitals. A recent survey done in England found that there is variable provision of home mechanical ventilation and sleep services, with the majority of units offering overnight oximetry; polysomnography was available only in 17% of units.<sup>13</sup>

We agree with the conclusions of the authors of the English survey that stated “the introduction of a national registry with standardization of diagnostic and treatment pathways will provide the clinical governance structure.”

Integration of different hospital and services in a specific clinical network, the so-called “hub and spoke” network, may help to provide the best care for this unique patients: respiratory function monitoring, identification of best candidates for NIV is the first step; acclimatization to ventilator and titration procedure is the second step; continuous home-care and monitoring is the final step. Care providers, both in- or out-hospital services, may offer all or a part of these procedures. However, specific criteria of accreditation should be defined by national health organizations.

## CITATION

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## DISCLOSURE STATEMENT

The authors have indicated no financial conflicts of interest.