

TREATMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME BY DIAPHRAGM PACING STIMULATION IN A PATIENT WITH AMYOTROPHIC LATERAL SCLEROSIS

Burcu Zeydan, Gülçin Benbir, Mehmet Ali Akalın, Derya Karadeniz

Istanbul University, Cerrahpasa School of Medicine, Department of Neurology, Istanbul

ABSTRACT

Obstructive sleep apnea syndrome (OSAS) is commonly seen in patients with neurological disorders, such as amyotrophic lateral sclerosis (ALS), especially later in disease course when diaphragmatic dysfunction and respiratory compromise becomes evident. The gold standard therapy of OSAS is the noninvasive mechanical ventilation (NIMV). The mainstay treatment for patients with ALS and respiratory disturbances is also accepted as NIMV to prolong life expectancy. Diaphragm pacing stimulation

(DPS) has recently been introduced and suggested to be beneficial in patients with ALS. Here we report a patient with ALS, in whom OSAS was completely resolved upon DPS intervention. With more common application of diaphragmatic pacing in ALS patients with respiratory involvement will offer a supportive treatment rather than traditional palliative care.

Keywords: Amyotrophic lateral sclerosis, obstructive sleep apnea syndrome, mechanical ventilation, diaphragm. *Nobel Med 2016; 12(1): 94-96*

AMİYOTROFİK LATERAL SKLEROZ OLGUSUNDA DİYAFRAM PİL UYARIMI İLE OBSTRÜKTİF UYKU APNE SENDROMUNUN TEDAVİSİ

ÖZET

Obstrüktif uyku apne sendromu (OUAS); amiyotrofik lateral skleroz (ALS) gibi nörolojik hastalığı olan hastalarda, özellikle hastalığın ileri dönemlerinde diyafram fonksiyonlarının bozulması sonucu solunumun etkilenmesine bağlı olarak sıklıkla görülmektedir. OUAS'nin altın standart tedavisi invaziv olmayan mekanik ventilasyon (NIMV) tedavisidir. Solunum etkilenmesi olan

ALS hastalarındaki ana tedavi de yaşam beklentisini artıran NIMV olarak kabul edilmektedir. Son zamanlarda diyafram pil uyarımı (DPU) tedavisi, ALS hastalarında yararlı bir tedavi olarak gündeme gelmiştir. Bu olgu sunumunda, DPU sonrasında OUAS'yi tam olarak gerileyen bir ALS hastası sunulmaktadır. Solunum etkilenmesi olan ALS hastalarında DPU'nun daha yaygın olarak kullanılması, geleneksel palyatif yaklaşıma kıyasla destekleyici bir tedavi seçeneği sunmaktadır.

Anahtar kelimeler: Amiyotrofik lateral skleroz, obstrüktif uyku apne sendromu, mekanik ventilasyon, diyafram. *Nobel Med 2016; 12(1): 94-96*

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive obstruction of the upper airway and oxygen desaturation episodes, which, in turn, result in several cardiovascular consequences and poor outcome.¹ OSAS is commonly seen in patients with neurological disorders, such as amyotrophic lateral sclerosis (ALS), especially later in disease course when diaphragmatic dysfunction and respiratory compromise becomes evident.^{2,3} Noninvasive mechanical ventilation (NIMV), the gold standard therapy of OSAS, has been shown not only to be effective on respiratory disturbances, but also to improve survival and quality of life in these patients.⁴ Diaphragm pacing stimulation (DPS), which induces inhalation by stimulating the inspiratory muscles, has recently been introduced and suggested to be beneficial in patients with ALS.^{5,6} Here we report a patient with ALS, in whom OSAS was completely resolved upon DPS intervention.

CASE

A sixty-three year-old male patient was admitted to our Sleep Disorder Unit complaining of difficulty in breathing during sleep for few months. He was diagnosed as amyotrophic lateral sclerosis about two years ago, and was on riluzole therapy (100 mg/day) since. His past medical history was otherwise unremarkable. His family history was unremarkable. His neurological examination revealed dysarthric speech and dysphagia; he had generalized weakness (muscle strength of 4/5); there was no other abnormal finding.

When questioned, he had mild to moderate snoring, witnessed apnea, nocturia (two to three times in a night), dry mouth upon awakening, gastro-esophageal reflux (few nights in a month) and morning headache. He also stated mild daytime sleepiness, with an Epworth sleepiness scale of 6 points. Pittsburgh sleep quality index was determined as 9 points. He denied any symptoms of restless legs syndrome, periodic legs movement disorder, parasomnias or REM (rapid eye movement) sleep behavior disorder.

A full-night polysomnographic (PSG) examination revealed that the apnea-hypopnea index (AHI) was 10 per hour and the respiratory disturbance index (RDI) was 16.1 per hour; which were more predominant in supine position. The average oxygen saturation was 95.1%, which decreased to as low as 89% with abnormal respiratory events. There was no phasic or tonic increases in REM tonus in chin electromyography (EMG). Bilateral leg EMG recordings showed fragmentary myoclonus. Electrocardiography showed brady-tachy arrhythmias associated with abnormal respiratory events, but otherwise normal.

The patient was diagnosed as obstructive sleep apnea syndrome and a second full-night PSG was performed two weeks later for BPAP (Bilevel positive airway pressure) titration. He was put on BPAP therapy with an oronasal mask; the pressures were set as an inspiratory pressure of 11 mmHg and an expiratory pressure of 7 mmHg, which controlled all abnormal respiratory events successfully in every positions and sleep stages. The mean oxygen saturation was observed as 95.3% in wakefulness and as 94.8% during sleep.

He was followed-up in outpatient clinic of Sleep Disorders Unit without any symptoms regarding OSAS for 15 months. During this period, however, his speech was further deteriorated and became very difficult to understand. As he had greater difficulty in swallowing, gastrostomy was performed. Otherwise, he was able to walk without any assistance with generalized muscle strength of 4/5. About four months ago, he developed progressive daytime shortness of breath and the indication for diaphragm pacing stimulation was made about three and a half years after the diagnosis of ALS, and 15 months after the initiation of BPAP therapy. Diaphragm pacing stimulation (NEURX DPS Diaphragm pace) was placed. For four months, the patient did not use BPAP therapy and he had no symptoms regarding OSAS. He was internalized for a full-night PSG recording, which revealed that AHI was 2.1 per hour and RDI was 4.1 per hour. The mean oxygen saturation was observed as 96.5% in wakefulness and as 95.5% during sleep. His body mass index was not changed; sleep parameters such as sleep efficiency or the percentage of REM sleep and the time he spent in supine position were all similar to those with BPAP therapy.

In the last visit about three months later, the patient was anarthric with no sound production. The muscle strength was 3/5 in his upper extremities allowing him to make some gestural movements, but he was unable to take self-care activities. The muscle strength in his lower extremities was 2/5; he was no longer able to walk without assistance and wheelchair-bound. He was fed via gastrostomy. There was no urine or fecal incontinence. His wife mentioned that he had shortness of breath, increased saliva and frequent coughing, which were present during daytime and at nights.

DISCUSSION

The mainstay treatment for ALS patients with respiratory insufficiency is accepted as NIMV to prolong life expectancy.⁶ The presented patient had the diagnosis of ALS and OSAS, who was effectively treated by NIMV (BPAP therapy). However, later in disease course, he developed daytime symptoms of respiratory dysfunction, upon which DPS was performed. There

**TREATMENT OF
OBSTRUCTIVE SLEEP
APNEA SYNDROME
BY DIAPHRAGM
PACING STIMULATION
IN A PATIENT WITH
AMYOTROPHIC LATERAL
SCLEROSIS**

is a close link between diaphragm function and sleep abnormalities, both in general and during ALS where diaphragm weakness is associated with deteriorated sleep architecture.^{7,8} Diaphragm pacing stimulation has now been introduced in patients with motor neuron disease or ALS.⁹ The pilot data suggested that DPS can positively influence diaphragm physiology, respiratory functions, and survival in these patients. DPS, by artificially replacing or supporting the affected pathways, improved respiratory functions both during wakefulness and during sleep.⁹ In addition to beneficial effects on overall respiratory functions of DPS, here we observed that DPS was also effective on obstructive sleep apnea in a patient with ALS.

Diaphragmatic pacing is known to be effective in central sleep apnea and primary alveolar hypoventilation syndromes.^{6,9} The effect of DPS on obstructive events, however, is not established. In patients with ALS, significant sleep improvements were established with DPS therapy irrespective of patients' status regarding NIMV.⁶ In that study, four months of diaphragm conditioning exhibited improved diaphragm endurance despite a loss of diaphragm strength. In our patient, PSG recordings following four months of DPS showed that obstructive sleep apnea syndrome was cured, with preserved sleep parameters as in BPAP titration night. With more common application of diaphragmatic pacing in ALS patients with respiratory involvement will offer a supportive treatment rather than traditional palliative care. This case illustrates the efficacy of diaphragmatic pacing on abnormal respiratory

events of obstructive type. Programmed diaphragmatic pacing using implanted neuromodulators represents an emerging method for providing pulmonary support using negative pressure ventilation.¹⁰ The implantable, rechargeable, programmable and miniaturized nature of diaphragmatic pacers may obviate many of the management issues associated with NIMV devices allowing wider adoption of ventilatory support and improve quality of life.

CONCLUSION

As this patient had amyotrophic lateral sclerosis in addition to OSAS, future studies should specifically address how diaphragmatic pacing will affect obstructive sleep apnea in general population. However, as DPS is an expensive and invasive procedure, it may be saved for patients with severe OSAS, or those with accompanying hypoventilation or central sleep apnea, who could not efficaciously be treated by or tolerate noninvasive mechanical ventilation. Comparative studies of NIMV and diaphragmatic pacing on the prognosis of underlying diseases would also be very informative in managing patients with chronic illnesses.

Acknowledgement

We have obtained informed consent from the patient. There is no financial support, off-label or investigational use.

* The authors declare that there are no conflicts of interest.

C	CORRESPONDING AUTHOR: Burcu Zeydan Istanbul University, Cerrahpasa School of Medicine, Department of Neurology, Istanbul, Türkiye drburcuzeydan@gmail.com
✓	DELIVERING DATE: 28 / 11 / 2014 • ACCEPTED DATE: 17 / 03 / 2015

REFERENCES

1. Park JG, Ramar K, Olson EJ. Updates on definition, consequences, and management of obstructive sleep apnea: Mayo Clin Proc 2011; 86, 549-554.
2. Hetta J, Jansson I. Sleep in patients with amyotrophic lateral sclerosis. J Neurol 1997; 244: 7-9.
3. 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.
4. Katzberg HD, Selegiman A, Guion L, et al. Effects of noninvasive ventilation on sleep outcomes in amyotrophic lateral sclerosis. J Clin Sleep Med 2013; 9: 345-351.
5. Mahajan KR, Bach JR, Saporito L, Perez N. Diaphragm pacing and noninvasive respiratory management of amyotrophic lateral sclerosis/motor neuron disease. Muscle Nerve 2012; 46: 851-855.
6. Gonzalez-Bermejo J, Morélot-Panzini C, Salachas F, et al. Diaphragm pacing improves sleep in patients with amyotrophic lateral sclerosis. Amyotroph Lateral Scler 2012; 13: 44-54.
7. Arnulf I, Similowski T, Salachas F, et al. Sleep disorders and diaphragmatic function in patients with amyotrophic lateral sclerosis. Am J Respir Crit Care Med 2000; 161: 849-856.
8. Ferguson KA, Strong MJ, Ahmad D, George CF. Sleep disordered breathing in amyotrophic lateral sclerosis. Chest 1996; 110: 664-669.
9. Onders RP, Elmo M, Kaplan C, Katirji B, Schilz R. Final analysis of the pilot trial of diaphragm pacing in amyotrophic lateral sclerosis with long-term follow-up: diaphragm pacing positively affects diaphragm respiration. Am J Surg 2014; 207: 393-397.
10. Yun AJ, Lee PY, Doux JD. Negative pressure ventilation via diaphragmatic pacing: a potential gateway for treating systemic dysfunctions. Expert Rev Med Devices 2007; 4: 315-319.