Sleep and Survival in Amyotrophic Lateral Sclerosis (ALS): The Parallelism in Motor and Non-Motor Progression

Sleep disruption is common among patients with amyotrophic lateral sclerosis (ALS) and contributes substantially to the disease burden.[1,2] Sleep quality of ALS patients may be affected by various contributory factors: motor symptoms of ALS (fasciculations, muscle cramps, immobilization, restless legs syndrome, and bulbar weakness), nocturnal pain (as a result of immobilization, muscle atrophy that enhances pressure load to bones and joints as well as neuropathic pain), sleep-related breathing disorders (mainly nocturnal hypoventilation and obstructive sleep apnea), and behavioral abnormalities during sleep (parasomnias and REM behavioral disorders).[3] Psychological factors such as depression and anxiety may lead to significant insomnia.[3] In addition, a genetic mutation in ALS has also been shown to play a role in sleep quality.[4] All the above conditions contribute to poor sleep quality which negatively impacted the already limited survival period of patients with ALS.

The majority of these contributing factors of sleep disruption are attributable to progressive motor deterioration in ALS and may occur at different stages of disease severity. Therefore, it is reasonable to evaluate sleep burden as ALS progresses. In this issue, Li X *et al*.[5] evaluated longitudinally the effect of sleep quality on disease progression in 63 patients with ALS over 12 months follow-up using Pittsburgh sleep quality index (PSQI) score. Comparing between good (PSQI ≤5) and poor sleepers (PSQI >5), they found that patient with poor sleep quality at diagnosis is associated with rapid deterioration of respiratory function (change in forced vital capacity (ΔFVC)) during disease progression. Although assessment using PSQI was subjective and prior determination of underlying sleep disorders was not performed, the result of this study represented the all-inclusive overall effect of sleep burden in ALS patients in the real world. Similar data from recent evidence support poor sleep quality as one of the clinical determinants among ALS patients directly related to disease severity.[6] This crucial information supports the understanding that sleep quality in ALS patients is not only due to individual sleep-related breathing disorders but rather multifactorial.

The novel approach of the study is clearly the longitudinal approach where the authors identified the patient at baseline and follow-up at 6 and 12 months for FVC change along with disease progression (the revised ALS functional rating scale, ALSFRS-R) in patients without respiratory insufficiency from the outset. This approach allowed parallel assessment of both parameters, providing the true clinical profile of sleep incidence as the disease progresses. The study found at baseline 38.1% of ALS patients were poor sleepers, and this percentage increased to 60.3% and 74.6% after 6- and 12-months follow-up. This is likely due to the compounded factors of both neurodegenerative processes of ALS and disruption in sleep amount and sleep fragmentation.[7] Nevertheless, this important finding underscores the pragmatic need for a continuous comprehensive sleep assessment throughout the course of ALS.

Neurodegenerative progression beyond the motor cortex and corticospinal tract to the involvement of the brainstem that is responsible for REM sleep and related neuronal networks controlling respiration and oculomotor function has been implicated in causing disorders of sleep and wakefulness in ALS.[8,9] While neuropathology of ALS remains the focus of future research for both motor and non-motor symptoms, more attention on early identification of sleep disorders among ALS patients should be of clinical priority in improving the overall quality of life and survival.

Hiew FL

Neurology Division, Medical Department, Sunway Medical Centre, Bandar Sunway, Selangor, Malaysia

Address for correspondence: Dr. Hiew FL, Consultant Physician and Neurologist, Sunway Medical Centre, No. 5, Jalan Lagoon Selatan, Bandar Sunway, 47500, Selangor, Malaysia.
E-mail: hiewfl@gmail.com

References

1. Lo Coco D, La Bella V. Fatigue, sleep, and nocturnal complaints in patients with amyotrophic lateral sclerosis. Eur J Neurol 2012;19:760-3.
2. Raheja D, Stephens HE, Lehman E, Walsh S, Yang C, Simmons Z. Patient-reported problematic symptoms in an ALS treatment trial. Amyotroph Lateral Scler Frontotemporal Degener 2016;17:198-205.
3. Boentert M. Sleep and sleep disruption in amyotrophic lateral sclerosis. Curr Neurol Neurosci Rep 2020;20:25.
4. Sun X, Zhao X, Liu Q, Liu S, Zhang K, Wang ZL, *et al*. Study on sleep-wake disorders in patients with genetic and non-genetic amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 2020. doi: 10.1136/jnnp-2020-324544.
5. Li X, Liu Q, Niu T, Jia H, Liu T, Xin Z, *et al*. Sleep disturbances as a potential risk factor for deterioration of respiratory function in patients with amyotrophic lateral Ann Indian Acad Neurol 2023;26:754-60.
6. Goudarzi A, Agah E, Ghajarzadeh M, Jazani MR, Sarraf P. Clinical determinants of sleep quality in patients with amyotrophic lateral sclerosis. Sleep Breath 2023. doi: 10.1007/s11325-023-02853-w.
7. Chauhan AK, Mallick BN. Association between autophagy and rapid eye movement sleep loss-associated neurodegenerative and patho-physio-behavioral changes. Sleep Med 2019;63:29-37.
8. Lucia D, McCombe PA, Henderson RD, Ngo ST. Disorders of sleep and wakefulness in amyotrophic lateral sclerosis (ALS): A systematic review. Amyotroph Lateral Scler Frontotemporal Degener 2021;22:161-9.
9. Turner MR, Al-Chalabi A. REM sleep physiology and selective neuronal vulnerability in amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 2020;91:789-90.

Submitted: 25-Jun-2023 **Accepted:** 25-Jun-2023
Published: 25-Sep-2023

DOI: 10.4103/aian.aian_562_23