CLINICAL AND POLYSOMNOGRAPHICAL EVALUATION OF SLEEP IN PATIENTS WITH CUSHING'S SYNDROME

Ismailogullari S[1], Firat ST[2], Karaca Z[2], Tanriverdi F[2], Unluhizarci K[2], Kelestimur F[2]
[1]Erciyes University Medical School Department of Neurology, Kayseri, Turkey
[2]Erciyes University Medical School Department of Endocrinology, Kayseri, Turkey

OBJECTIVES

Disturbed sleep is a frequent symptom in Cushing's Syndrome (CS). Few studies have evaluated sleep in CS using polysomnography (PSG). In these studies, decreased N3 sleep, disturbances of sleep continuity and REM sleep disinhibition were reported in CS patients [1,2]. However; the prevalance of sleep disorders like, obstructive sleep apnea syndrome, restless legs syndrome (RLS), insomnia and hypersomnia have not been explored yet. The aim of the present study was to evaluate the prevalance of sleep disorders clinically and the sleep structure using PSG in patients with CS.

Table 1: Prevalance of sleep disorders in patients with Cushing's syndrome and control group

Sleep disorders	Cushing's syndrome N=33	Control group N=20	p
Obstructive sleep apnea (AHI>5) Severe obstructive sleep apnea (AHI>15)	17 (51.1%) 7 (21%)	5 (25%) 2 (10%)	0.114
Periodic limb movements of sleep (PLMI>15)	5 (15%)	52 (25%)	0.295
Insomnia	20 (60%)	0*	*
Restless Legs Syndrome	2 (6.1%)	0*	*
Hypersomnia	0 (0%)	0*	*

*Insomnia, hypersomnia and restless legs syndrome were excluded in the control group before enrollment. So no comparison was done.

Table 2: PSG parameters in patients with Cushing's syndrome and control group

	Cushing's syndrome n=15	Control group n=13	p
Total sleep time (min)	297.9±104.0	354.8±52.8	0.087
Sleep latency (min)	20.0±12.7	14.6±13.4	0.555
Sleep efficiency (%)	74.3±24.9	85.6±8.3	0.235
WASO (min)	97.8±43.9	44.3±28	0.413
Stage N1 sleep (%)	12.8±3.1	7.3±2.9	0.121
Stage N2 sleep (%)	65.3±11.3	54.4±13.3	0.028
Stage N3 sleep (%)	12.4±3.0	23.3±4.5	0.052
Stage R sleep (%)	12.8±5.9	14.9±5.3	0.357
Arousal index (n/hour)	4.7±1.3	6.6±4.9	0.310
AHI (n/hour)	1.5±0.98	1.8±1.4	0.394
Minimum O_2 saturation	84.9±3.7	85.8±11	0.765
PLMI (n/hour)	9.3±6.7	9.1±5.5	0.932
Average heart rate	73.6±6.8	65.6±7.5	0.006
Minimum heart rate	58.8±6.1	51.8±7.6	0.013
Maximum heart rate	108.3±9.5	102.7±9.9	0.147

METHODS

Thirty three patients with CS were evaluated both clinically and with PSG findings in terms of sleep disorders and data were compared with 20 healthy controls without any sleep complaints. Insomnia and RLS were diagnosed according to ICSD-3 [3]. Epworth Sleepiness Scale score ≥10 was accepted as hypersomnia. Sleep parameters were evaluated after exclusion of sleep apnea and periodic limb movements (PLM) of sleep.

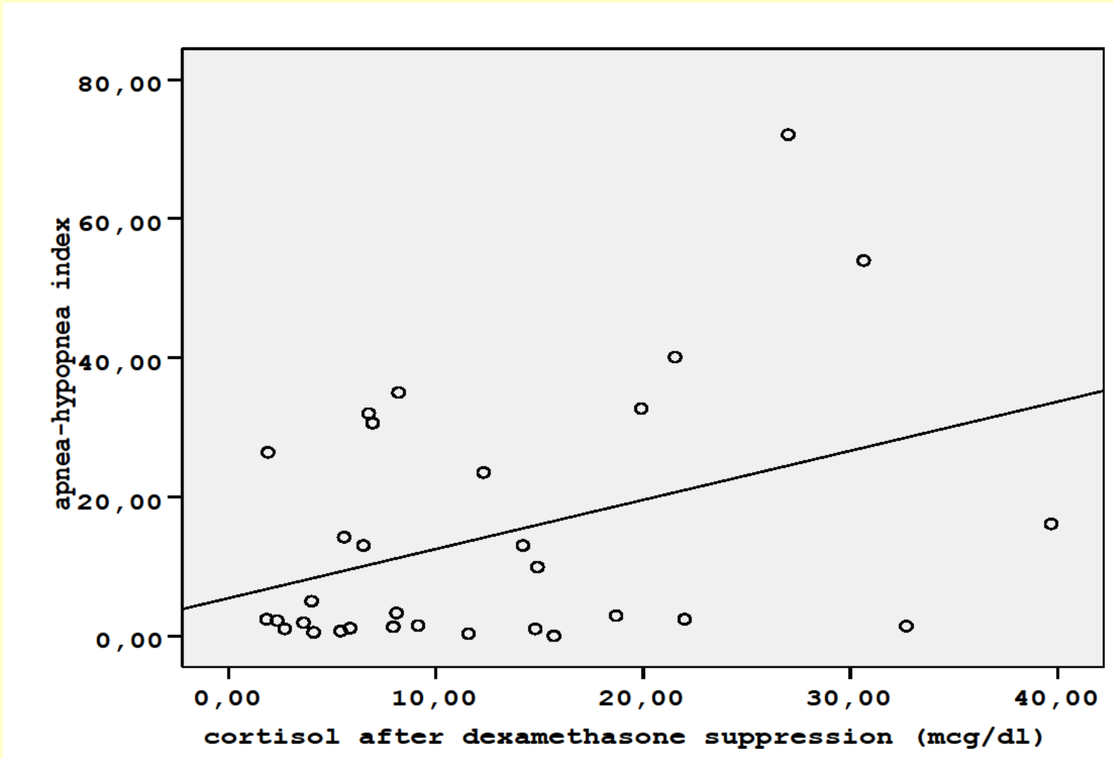

Figure 1: Correlation of apnea-hypopnea index with cortisol after low dose dexamethasone supression test

RESULTS

Seventeen (51.1%) patients with CS demonstrated sleep apnea (Apnea Hypopnea Index [AHI]≥5), with seven (21%) of 17 had severe sleep apnea (AHI≥30). Five (15%) patients had PLM of sleep (PLM Index≥15), 20 (60%) patients had clinical insomnia, and two (6.1%) patients had RLS. None of the CS patients complained of hypersomnia (Table 1). PSG parameters were compared only if participants had an AHI<5 and PLMI<15. The percentage of stage N2 sleep was significantly increased in CS patients compared to control subjects. Although total sleep time and percentage of time spent in stage N3 sleep was reduced in CS patients, the difference was not statistically significant. Average heart rate and minimum heart rates were significantly higher in CS patients (Table 2). There was a significant positive correlation between post-dexamethasone cortisol levels and AHI (Figure 1), and midnight cortisol levels and AHI in REM sleep. Minimum O_2 saturation was found to be negatively correlated with midnight and basal cortisol levels.

CONCLUSIONS

Patients with CS, as well as those with exogenous glucocorticoid excess, often complain about sleep disruptions. Previous studies assessing sleep in patients with CS demonstrated the detrimental effects of high glucocorticoid levels on sleep quality using EEG only or PSG[1,2].
In this study we evaluated sleep disorders clinically for the first time, additionally sleep structure using PSG. Insomnia and sleep apnea are frequent sleep disorders in CS patients. Absence of hypersomnia, alterations in sleep structure and higher heart rate during sleep support a hyperarousal state in CS. As insomnia and OSA have been shown to increase the risk of developing cardiovascular diseases [4-5], it is conceivable that the cardiometabolic profile of patients with CS may be worsened by impaired sleep and a physiological hyperarousal state.

REFERENCES

1. Krieger DT, Glick SM (1974) Sleep EEG stages and plasma growth hormone concentration in states of endogenous and exogenous hypercortisolemia or ACTH elevation. J Clin Endocrinol Metab 39(6):986–1000
2. Shipley JE, Schteingart DE, Tandon R, Starkman MN (1992) Sleep architecture and sleep apnea in patients with Cushing's disease. Sleep 15(6):514–518
3. American Academy of Sleep Medicine. International Classification of Sleep Disorders, 3rd ed. Darien, IL (ICSD-3): American Academy of Sleep Medicine, 2014.
4. Pannain S, Beccuti G, Van Cauter E (2012) The connection between sleep loss, obesity, and type 2 diabetes. In:hiromani P, Horvath T, Redline S, Van Cauter E (eds) Sleep loss and obesity: intersecting epidemics. Springer, New York, pp 133–168
5.Dong JY, Zhang YH, Qin LQ (2013) Obstructive sleep apnea and cardiovascular risk: meta-analysis of prospective cohort studies. Atherosclerosis 229(2):489–495