National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Comparison of sleep in hypothyroid patients with normal controls

Kavitha Sivaprakasam, Shanthimalar Ramamoorthy

Department of Physiology, Madras Medical College, Chennai, Tamil Nadu, India

Correspondence to: Kavitha Sivaprakasam, E-mail: drkavitha2010@yahoo.co.in

Received: February 16, 2017; **Accepted:** June 27, 2017

ABSTRACT

Background: Sleep - A complex amalgam of behavioral and electrophysiological process is maintained by organized interaction between neurons, neural circuits, and neurotransmitters. Hypothyroidism is the inadequate secretion of thyroid hormones by the thyroid gland. Hypothyroidism, the 2nd common endocrine disorder, is often accompanied by complaints of daytime fatigue. This chronic fatigue should be managed as it may result in impaired attention with adverse consequences in the classroom, workplace, not to forget the highways. **Aims and Objectives:** The primary focus of the present study is to evaluate sleep cycle in newly diagnosed overt hypothyroid patients to investigate if this fatigue is the consequence of sleep disorder. **Materials and Method:** A total of 30 hypothyroid patients of both sexes underwent polysomnography to assess sleep based on bioelectric potentials - electroencephalogram, electromyogram, and electrooculogram. The results were compared with age- and sex-matched euthyroid controls. **Results:** Hypothyroid patients showed significant changes in sleep stages when compared with normal euthyroid controls. Although their total sleep time was not significantly altered, Stage I and Stage II sleep was significantly increased ($P < 0.001$) while deep sleep and rapid eye movement sleep were reduced. **Conclusion:** This research proves that early diagnosis of hypothyroidism and management guarantees an improvement in sleep quality and productivity in life.

KEY WORDS: Hypothyroid; Polysomnography; Sleep Stages

INTRODUCTION

Sleep is an enigma - a unique, active process with both quantitative and qualitative dimension that influences immunity, thermoregulation, metabolism, hormonal levels, and last but not the least, higher functions of memory, cognition, and judgment. During sleep consolidation and integration of new memories without the interference of any ongoing activities takes place.[1] At the cellular level, sleep replenishes the glycogen stores in glial cells. The toxic free radicals accumulated during wakefulness are removed during sleep.[2] Sleep disorder is defined as disruption in pattern of sleep. It includes difficulty in falling asleep, staying asleep, excessive total sleep time, falling asleep at inappropriate times, and/or abnormal behaviors associated with sleep. Hypothyroid patients sleep for long periods during the day and when hypothyroidism is severe may lapse into stupor and even coma.[3] In spite of such long sleep period, they tend to wake up unrefreshed and remain lethargic throughout the day. The focus of this work is to study the effect of deficient thyroid hormones on nocturnal sleep pattern in overt hypothyroid people.

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2017.7.0203427062017	

Objective

The primary objective was to evaluate the sleep pattern by observing the sleep stages in hypothyroid patients in comparison with age-and sex-matched normal euthyroid controls. This study was also aimed to investigate the impact of thyroid hormone deficiency on sleep efficiency.

MATERIALS AND METHODS

This study was conducted at the Institute of Physiology and Experimental Medicine, Madras Medical College. After obtaining approval of the study from the Institutional Ethical Committee, 30 patients with thyroid profile showing overt hypothyroidism were selected from both sexes between the age group of 18 and 50 years. 30 age-and sex-matched controls were selected for comparison with the cases.

After reviewing the patient's symptoms, family history, and physical examination, diagnosis of hypothyroidism was done by enzyme-linked immunosorbent assay of serum thyroid stimulating hormone (TSH), serum total thyroxine, and serum triiodothyronin using ERBA Thyrokit. Fasting blood samples were collected to reduce pre-analytical variability and to minimize influence caused by food.[4]

The normal standardized values are:
- Serum TSH: 0.5-5.5 mIU/L
- Serum total thyroxine: 40-120 nmol/L
- Serum total triiodothyronin: 0.8-2 ng/mL.

The TSH levels had a mean value of 103.02 ± 28.16 in hypothyroid patients. This is of great significance when compared to 2.74 ± 1.03 in controls indicating that the patients belonged to the overt hypothyroid category.

Cases and controls underwent a full night polysomnography (PSG) study using RMS polygraph machine (Recorders and Medicare Systems Private Limited Company).

Inclusion Criteria

Newly diagnosed overt hypothyroid patients not on thyroxine replacement between the age group 18 and 50 years of both sexes with regular night time sleep habits were selected.

Exclusion Criteria

Nightshift workers with irregular sleep routine, diabetes mellitus, hypertension, anemia, renal failure, neurological and psychiatric disorders, substance abuse, gastroesophageal reflux disease, ear, nose, and throat T disorders, and cardiopulmonary disorders were excluded from the study. Individuals on antihistamines, steroids, analgesics containing caffeine or alcohol, and medications that interfere with sleep patterns were also excluded from this study. Salt causes disruption in normal sleep pattern. Non-rapid eye movement (REM) decreases and REM increases so they dream a lot and even experience nightmares.[5] Hence, the participants were recommended to abstain from taking food with high salt content such as chips and pickles in the evenings.

Controls were age-and sex-matched individuals with normal healthy sleep hygiene. 15 males and 15 females-with normal thyroid profile were designated as "control" and hypothyroid patients - 15 males and 15 females were listed as "case". Although hypothyroidism has increased incidence in females, an equal gender distribution was opted to minimize the effect of sex hormones on sleep in this study. Testosterone reduced total sleep time by direct central nervous system effects by altering serotonergic neurotransmission.[6] Testosterone also increased metabolic rate, impairing sleep quality.[7]

After explanation of the procedure, informed verbal and written consent was obtained from the participants, to PSG was recorded.

Pre-study Procedure

All participants had to adhere to the following set of instructions: Shave, take bath in the evening, not apply oil, take dinner at least 1 h before sleep study, not consume alcohol on the day of the study, avoid coffee or tea at least 3 h before the study, dress in routine sleepwear, remove all ornaments, and report for sleep study at the appointed time. They were asked to maintain their usual sleeping pattern and avoid daytime naps on the day of the study. The participants were made to feel comfortable with the laboratory and sleep study process to ensure maximum compliance during the study.

International 10-20 system was used for recording electroencephalogram (EEG), the prime variable to document sleep stages, wakefulness, and arousals during sleep. The channels (C4-A1, Fpz-A1, and O2-A1) were used for evaluating waveforms.[8] Additional channels (C3-A2, Fpz-A2, and O1-A2) were recommended to provide redundancy in case of electrode malfunction.[9] Electrooculogram (EOG) derivations were E1 - Fpz and E2 - Fpz. Submental EMG was recorded.

At the start of the study, physiologic biocalibrations were performed to ensure optimal signal to maximize amplitude, take advantage of common mode rejection, and prevent impedance mismatch. The standard electrode impedance upper limit is 5 k ohms for EEG and EOG[10] whereas it is 10 k ohms for EMG.[11] The electrode discs were secured to the sites using electrode paste.

After ensuring that all sensors and equipment were functioning properly, the recording was started. "Lights out" and "lights on" times were documented. The patient's clinical status and body position were monitored and any change in sleep pattern was documented. A 6-8 h PSG recording was obtained.

Scoring and analysis of recorded data were done using the sleep scoring criteria of Rechtschaffen and Kales,[12] in concordance with the updates given by the American Academy of Sleep Medicine.[13]

Statistical Methodology

The data collected were statistically analyzed using Student's independent *t*-test to compare the means and standard deviations between the 2 groups. The $P < 0.05$ was taken as statistically significant.

RESULT

Total sleep time in both hypothyroid and euthyroid individuals are not statistically significant - the mean value in cases being 399 ± 18.68 and control being 395 ± 21.20. However, the sleep efficiency percentage of hypothyroid patients shows a significant decrease with a mean value 84 ± 7.05 when compared to euthyroid controls' value of 92.55 ± 2.17 ($P < 0.001$). Sleep efficiency percentage is the percentage of total sleep time to the total recording time, normal value being more than 90% (Figure 1).

Sleep Stage I of hypothyroid patients was significantly longer 43.87 ± 10.88 (euthyroid 21.83 ± 7.22). The percentage of sleep Stage I is inversely related to sleep continuity. Stage II sleep in hypothyroids was significantly increased 222.52 ± 20.25 (euthyroid 207 ± 18.45). Stage III and IV was reduced in hypothyroid patients 18 ± 3.97 (euthyroid 20.18 ± 3.84) though not significant statistically. Sleep latency was scored as the duration between "lights out" and sleep onset, defined by the 1st 3 consecutive epochs of Stage I. The sleep onset latency measured in minutes of hypothyroid patients' 6.16 ± 2.78 shows a significantly decreased $P < 0.001$ when compared to euthyroid controls 12.60 ± 2.48 (Table 1).

Other studies relating to the current work show increased sleep latency, reduced total sleep time, increased REM density, and REM duration with reduction in slow-wave sleep (SWS) in few patients with clinical hyperthyroidism:[14] reduced sleep efficiency, low delta sleep, short REM latency, and high REM density in one case of thyrotoxicosis;[15] higher percentage of SWS during hyperthyroid state as compared to sleep structure, once the thyroid hormone levels had returned to normal;[16] very low SWS in patients with hypothyroidism;[17] and 6 clinical hypothyroid patients with increase in sleep Stage II and reduction of SWS. The SWS reportedly returned to normal on hormone replacement therapy.[18]

DISCUSSION

Although all the participants slept for nearly equal period, the quality of sleep given by sleep efficiency percentage was significantly reduced in hypothyroid patients proving sleep disruption. The reduced sleep efficiency in EEG[19] and autonomic arousals secondary to apneic spells, a sign of obstructive sleep apnea (OSA), is further accentuated by hypothyroidism.[20] In addition to wake-to-sleep transition, sleep Stage I occurs during transitional stage during the entire sleep period. Being a stage

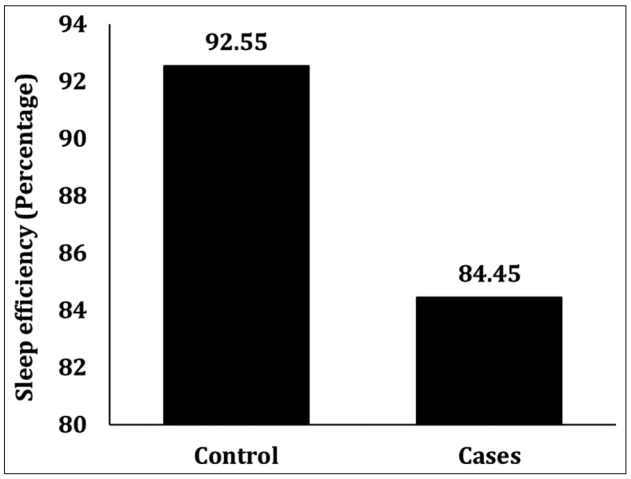

Figure 1: Comparison of sleep efficiency between control and hypothyroid patients

Table 1: Comparison of sleep stage percentages between control and hypothyroid patients

Variable	Group	Mean±SD	*P*-value
Stage I (min)	Control	21.83±7.22	<0.001**
	Cases	43.87±10.88	
Stage II (min)	Control	207.7±18.45	0.004*
	Cases	222.52±20.25	
Stage III and IV deep sleep (min)	Control	80.17±17.51	0.09
	Cases	72.6±16.93	
REM (min)	Control	85.83±15.95	<0.001**
	Cases	60.73±13.92	

SD: Standard deviation, REM: Rapid eye movement. *P<0.05; **P<0.001

of light sleep from which an individual can be easily aroused, this increase in duration of sleep Stage I and lack of deep sleep makes the hypothyroid patient feel unrefreshed and lethargic even after an adequate 8 h nocturnal sleep period.[18]

Deep sleep is necessary for progressive recovery and stabilization of synaptic junctions needed in "plastic" activities of learning, memory, and consciousness thus establishing sleep's function in neuronal recovery. Increasing TSH levels inhibits SWS.[21] Difficulty waking up in the morning or staying alert all day signifies that adequate time is not spent in different sleep stages, especially SWS and REM sleep. REM density indicated by maximal capacity for sleep is an index of sleep satiety.[22] Hypothyroidism is accompanied by increase in numbers of awakenings and reduction in amount of SWS.[23]

This study substantiates that hypothyroid patients suffer from sleep disturbance. Therefore, the inhibitory effect of sleep on TSH is lost aggravating the pathology to a greater extent.

Sleep disorders are of high medical and socioeconomic relevance, and hence adequate appraisal and treatment are

essential. Poor sleep is detrimental to both physical and psychological well-being and will impair waking functions.[28] It leads to impaired cognitive and psychomotor skills, utilizes health-care resources, impacts daytime productivity, and causes higher motor vehicle crashes.[29]

As PSG is time-consuming and costly, effective pre-clinical diagnostic procedures are needed. Knowledge as to which disorders could cause sleep disturbances and which diseases present initially as a sleep disorder would be helpful in managing the participants and in reducing the costs of diagnostic procedures and treatment by improving the diagnostic rationale. Furthermore, as poor sleep causes exacerbation of endocrine conditions, it is important that patients with endocrine and metabolic disorders be screened for habitual sleep patterns and OSA.[30]

This study does not support routine PSG - An expensive and time-consuming procedure to diagnose sleep disorder in hypothyroid patients. However, the importance of recording the history of sleep habits must be made mandatory to suspect sleep disorders at the clinical level. The impact of this study might have been improved by studying the sleep pattern following hormone replacement therapy and hence confirming the role played by thyroid hormone in achieving quality sleep.

CONCLUSION

Decreased thyroid hormone level is detrimental to (sleep quality) quality time spent in sleep due to frequent arousals, more time being spent in light superficial sleep and lack of sufficient deep and REM sleep. Sleep efficiency percentage in PSG can be considered as an indirect marker of sleep quality. Therefore, understanding the architecture of sleep, endogenous causes of sleep disruption, identifying and treating the underlying deficiency, will go a long way in helping the participants attain the quantity and quality of sleep needed.

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How to cite this article: Sivaprakasam K, Ramamoorthy S. Comparison of sleep in hypothyroid patients with normal controls. Natl J Physiol Pharm Pharmacol 2017;7(10):1127-1131.

Source of Support: Nil, **Conflict of Interest:** None declared.