Isolated Thyrotropin Elevation is Associated with Insufficient Night-sleep in Night-sleep Restricted Subjects

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Mild thyroid stimulating hormone (TSH) elevations are highly prevalent whereas large proportion of individuals with TSH elevations is without chronic autoimmune thyroid diseases. TSH secretion exhibits a daily circadian rhythm, and we previously reported that individuals with sleep disorders have significantly higher TSH levels than controls.[1] In this study, we evaluated the ratio of isolated TSH elevation in individuals with night-sleep restricted and re-evaluate which when night-sleep was recovered.

Nurses with or without night shift work were respectively recruited as the research group (Group A) or the control group (Group B). Individuals with thyroid disorders, chronic autoimmune thyroid diseases, neck surgery, radiotherapy, or suffering from diabetes mellitus, renal insufficiency, or <1 year postpartum were excluded. All nurses provided written informed consent, and the study was approved by the Biomedical Ethics Committee of our hospital, China (5101070022002).

Nurses in Group A were on duty for night shift work from 02:00 A.M. to 08:00 A.M. once a week, and then for 5–6 daytime work shifts after the night shift work. The night-sleep was considered being restricted at night shift work, and being recovered at daytime work. Blood samples of Group A were respectively collected at the end of night shift work (Group A-1) and daytime work (Group A-2). Blood of Group B were collected during the workday. All blood samples were collected between 08:00 A.M. and 11:00 A.M.

Serum levels of TSH, free triiodothyronine (FT3), free thyroxine (FT4), and thyroid peroxidase antibody (TPOAb) were measured in an electrochemiluminescence immunoassay (Roche Cobas 602, Mannheim, Germany). The reference ranges were as follows: TSH, 0.27–4.20 mU/L; FT3, 3.60–7.50 pmol/L; FT4, 12.0–22.0 pmol/L; and TPOAb <34 IU/ml (For TSH, the variation coefficients were between 2.0% and 3.5%; FT3, between 2% and 4%; and FT4, between 2% and 4%; TPOAb, between 5% and 12%). Isolated TSH elevation was defined as TSH >4.2 mU/L, with normal FT3 and FT4 levels. Chronic autoimmune thyroid diseases were diagnosed if TPOAb was >68 IU/ml.

Data processing was performed by SPSS 16.0 (SPSS Inc., Chicago, IL, USA). All data were reported as mean ± standard deviation (SD), percentage and P50 (P25, P75) as appropriate. *T*-test, Fisher's exact test, and rank sum test were compared of quantitative variables. A value of $P < 0.05$ was considered statistically significant.

Totally, 56 individuals in Group A and 28 individuals in Group B were included. No significant differences in age (25.70 ± 0.38 vs. 25.96 ± 1.15, $P = 0.826$), the ratio of females (54/56 vs. 28/28, $P = 0.550$), or body mass index (19.89 ± 0.28 vs. 19.80 ± 0.42, $P = 0.85$) were found between Group A and Group B.

Among Group A, 29% (16/56) had isolated TSH elevation at night shift work (Group A-1), and the ratio of that TSH elevation returned to be normal was 94% (15/16) at daytime work (Group A-2). The ratio of isolated TSH elevations in Group A-1 was significantly higher than that in Group A-2 (Fisher's exact test, 29% vs. 2%, $P = 0.002$). However, the proportion of isolated TSH elevation

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Table 1: Comparison of thyroid hormone at the time of night shift work, daytime work of night shift work nurses, and day-work of nurses without night shift work

Items	Group A-1 (n = 56)	Group A-2 (n = 56)	Group B (n = 28)	P*	P†
TSH (mU/L)	3.22 (2.40, 4.46)	2.20 (1.54, 2.87)	2.06 (1.57, 2.73)	<0.001	0.747
FT3 (pmol/L)	5.11 (4.73, 5.53)	4.88 (4.64, 5.15)	4.68 (4.51, 5.06)	0.001	0.160
FT4 (pmol/L)	16.87 (15.42, 17.59)	15.880 (14.95, 17.17)	16.33 (14.85, 17.52)	<0.001	0.809

*P: Group A-1 versus Group A-2; †P: Group A-2 versus Group B. Group A-1: Night shift work of nurses with night shift work; Group A-2: Daytime work of nurses with night shift work; Group B: Day-work of nurses without night shift work. TSH: Thyroid stimulating hormone; FT3: Free triiodothyronine; FT4: Free thyroxine.

was not significantly different between Group A-2 and Group B (Fisher's exact test, 2% vs. 4%, $P = 0.0558$).

Among Group A, the serum levels of TSH, FT3, and FT4 were significantly higher in Group A-1 than Group A-2 (rank sum test, data shown as P50, P25, and P75, [Table 1]). In addition, no significant differences in serum TSH, FT3, and FT4 levels were found between Group A-2 and Group B [Table 1].

In this study, the incidence of isolated TSH elevation was significantly increased when night-sleep was restricted. Mild TSH elevation tends to be diagnosed as subclinical hypothyroidism, whereas all participants in this study did not have thyroid diseases. In obstructive sleep apnea (OSA), the prevalence of elevated TSH and normal T4 was significantly higher than that in non-OSA.[2] OSA patients had short sleep duration and worse sleep quality, and the mean apnea duration was positively correlated with the TSH concentration. Mild TSH elevation in OSA patients may be associated with a short night-sleep duration or sleep disorder. Furthermore, 94% of the individuals with isolated TSH elevation at the time of night-sleep restriction had normal serum TSH concentrations at the time of night-sleep recovery. The results of our study suggested that isolated TSH elevation may be associated with night-sleep loss in insufficient night-sleep individuals without autoimmune thyroid diseases.

Moreover, this study showed that TSH level was significantly elevated and accompanied by elevated FT4 and FT3 concentration when night-sleep was restricted, which was consistent with the results reported by Aydin *et al*., who found that healthy controls had elevated TSH, T4, and T3 levels after one night of total sleep loss compared with baseline levels.[3] Similarly, serum TSH and T3 levels were significantly increased after one night of sleep loss in the healthy controls.[4] All these results suggested that TSH elevation when night-sleep is insufficient may be secondary to the homeostatic disequilibrium of the hypothalamic-pituitary-thyroid axis, which further elevates the serum level of FT4 and FT3.

The present study further revealed that TSH and FT4 levels at the time of night-sleep recovery were not significantly different from those of the controls. A previous study reported that in patients with primary insomnia, concentrations of TSH, T3, and T4 were significantly decreased after insomnia treatment.[5] Therefore, physicians are encouraged to collect a detailed sleep history if individuals have occasional, mildly isolated TSH elevation, especially if TPOAb is negative.

In conclusion, this study demonstrated that the ratio of isolated TSH elevation was increased, accompanied by elevated FT3 and FT4 levels within the reference range when night-sleep was restricted, whereas elevated TSH levels could be to be normal when night-sleep was recovered.

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Conflicts of interest

There are no conflicts of interest.

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