THE RELATIONSHIP BETWEEN DIURNAL VARIATION OF TSH AND THYROID BLOOD FLOW WITH DOPPLER ULTRASONOGRAPHY IN HEALTHY ADULTS

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INTRODUCTION

Thyroid stimulating hormone (TSH) shows pulsatile and circadian variation. In normal adult men and women, TSH levels are low throughout the daytime and begin to increase in the late afternoon or early evening. Maximal TSH levels occur shortly before sleep. During sleep, TSH levels generally decline slowly. A further decrease occurs in the morning hours. Thyroid gland is highly vascular, and TSH is known to alter the blood flow of the thyroid. It has been reported that measurement of blood flow at the inferior thyroid artery (ITA), a major feeding artery in the thyroid, is a useful method of differentiating between various thyroid diseases. However, there is no detailed study in the literature on the associations between the Doppler parameters of thyroid blood flow and diurnal rhythm of TSH.

The aim of present study was to determine the presence of a correlation between the Doppler parameters of thyroid blood flow and TSH levels in the morning, late afternoon and at midnight in healthy adults.

SUBJECTS AND METHODS

We prospectively examined 30 non- smoker healthy adults (15 men (50%) and 15 women (50%), 24- 54 years old). The sex, age, body weight, height and body mass index (BMI) were determined.

Blood samples were taken from individuals at 08.00 for measuring thyroid hormones [free triiodothyronin (FT3) and free thyroxine (FT4)], thyroid antibodies [anti thyroid peroxidase antibody (anti-TPO) and anti thyroglobulin antibody (anti-Tg)] and TSH levels. Thyroid hormones and TSH levels also were measured at 16.00 and 24.00. Subjects were required to collect 24-hour urine samples after discarding first urine sample in the morning. Daily iodine excretion was calculated from urine samples. Normal values in our laboratory are as follows: FT4, 0.61- 1.12 ng/dL; FT3, 1.57- 4,71 pg/mL; TSH, 0.4- 4.0 ulU/mL; anti-Tg <30 U/mL; anti-TPO <10 U/mL and Urine iodine 10- 20 µg/dL.

Conventional and Power Doppler Ultrasonography

Thyroid ultrasonography and Doppler ultrasonography was performed at 08.00, 16.00 and 24.00. In each individual, a preliminary ultrasonography examination was performed to identify any abnormalities such as parenchymal heterogeneity or nodule. All participants were examined after a 10- min rest period to minimize the changes in blood pressure and heart rate to avoid influencing the Doppler parameters. All Doppler and gray-scale measurements were performed by the same experienced radiologist (M.G) using the same Doppler ultrasonography device (Logic® 9 Doppler System, General Electric Medical Systems, Milwaukee, WI, USA) with a 10 MHz broadband linear transducer in thyroid mode. Thyroid gland was scanned in three dimensions. Thickness, width (in transverse plan), and length (in longitudinal plan) of each lobe were measured by longitudinal and transverse scans. Volume for each lobe was calculated using the ellipsoid formula. After the gray-scale ultrasonography examination, each individual underwent Doppler ultrasonography examination. Thyroid blood flow measured at the ITA, because of its major contribution to thyroid blood flow, ease of identification, and low coefficient of variation of less than 5.2%. The color gain was adjusted so that artifacts were prevented. The angle was kept between 45° and 60°, and the angle correction cursor was parallel to the direction of flow. The velocity waveform was displayed above the baseline to indicate the arterial blood flow, and the peak systolic velocity (PSV) and resistance index (RI) were obtained from both ITAs, and the mean values were recorded (Figure 1).

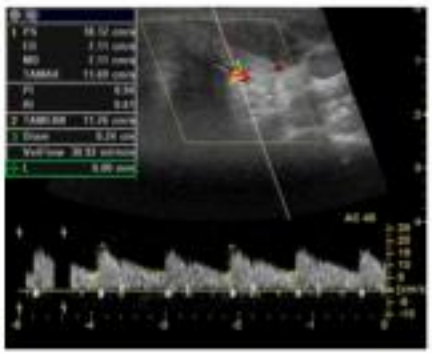

Figure 1. The velocity waveform is displayed above the baseline to indicate the arterial blood flow. The figure shows the measurement of the blood flow velocity in the inferior thyroid artery (left).

Statistical analysis

For the statistical analysis of the study, SPSS 11.5 packet program (SPSS Inc., Chicago, IL) was used. Values of $P < 0.05$ were accepted as statistically significant.

RESULTS

Thirty individual were included in the study between 24 and 54 years of age. There were 15 female (50%) and 15 male (50%) patients with a mean age of 32.20 ± 7.39 years. Mean BMI 24.70 ± 3.80 kg/m^2, and the mean urinary iodide excretion 14.07 ± 2.53 µg/dL were. Demographic and laboratory data of study group with comparative results according to sex were listed in Table I. No statistically significant difference was detected between groups according to age, BMI, thyroid function tests, and urinary iodine excretion ($p>0.05$).

Data of mean age, body mass index, FT3, FT4 and TSH levels, thyroid volumes, peak systolic velocity and resistance index at 08.00, 16.00 and 24.00 were showed in Table II. Diurnal serum TSH concentrations were evaluated and significant difference between morning, afternoon, and night TSH levels was detected. TSH levels measured at 24.00 were significantly high compared to those at 08.00 and 16.00 ($p<0.001$ and $p<0.001$, respectively). TSH levels measured at 16.00 were also significantly higher than those at 08.00 ($p<0.001$).

Diurnal thyroid volume changes were evaluated. There was no meaningful difference between thyroid volumes calculated from morning and afternoon measurements ($p=807$). However, thyroid volumes at night were significantly higher compared to morning and afternoon levels ($p<0.001$).

Mean PSV levels were evaluated and an increase during daytime was observed. However, no statistically significant difference was present between PSV values measured at 08.00 and 16.00 ($p=0.113$). PSV values measured at 24.00 were significantly high compared to morning and afternoon measurements ($p<0.01$, and $p<0.05$, respectively). In contrast to PSV, RI values tended to decrease during daytime. RI values measured at night were significantly low compared to morning and afternoon values ($p<0.001$). The difference between morning and afternoon RI levels were also statistically significant.

Table I. Demographic and laboratory data of study group with comparative results according to sex

	Male N=15	*Female N=15*	*P*
Age (year)	33 ± 8.5	31.3 ± 6.0	>0.05
BMI (kg/m^2)	25.5 ± 3.0	23.8 ± 4.4	>0.05
Urine iodine (µg/dL)	16.36 ± 3.01	15.04 ± 2.74	>0.05
FT3	3.24 ± 0.26	3.05 ± 0.85	>0.05
FT4	0.81 ± 0.07	0.79 ±0.05	>0.05
TSH	1.18 ± 0.64	1.32 ± 0.69	>0.05
Anti TPO (U/mL)	<10	<10	-
Anti Tg (U/mL)	<30	<30	-

Table II. Data of FT3, FT4 and TSH levels, thyroid volumes, peak systolic velocity and resistance index at 08.00, 16.00 and 24.00

	08.00	*16.00*	*24.00*
FT3 (pg/mL)	3.11 ± 0.59	3.00 ± 0.43	3.33 ± 0.63
FT4 (ng/dL)	0.77 ± 0.09	0.83 ± 0.08	0.86 ± 0.09
TSH (ulU/mL)	1.29 ± 0.55	1.88 ± 1.08	3.09 ± 1.52
Thyroid volume (mL)	10.46 ± 3.71	10.43 ± 3.75	12.02 ± 5.03
PSV (cm/s)	24.90 ± 8.51	25.88 ± 9.82	27.75 ± 9.54
RI	0.57 ± 0.07	0.56 ± 0.05	0.53 ± 0.07

CONCLUSION

Unique feature of our study is that it is the first study showing thyroid blood flow variations by quantitative Doppler parameters in relation to diurnal changes of TSH levels. In this study, we investigated the correlation between ITA blood flow parameters and thyroid volume, thyroid hormones, and TSH in three different times of day. We observed that PSV increased and RI decreased in night times when TSH peaked, which means increased thyroid blood flow. Again, we observed an increase in thyroid volume at night compared to daytime. Our study constitutes the beginning of the hypothesis that blood flow pattern in thyroid gland pathologies may show diurnal variation as in healthy individuals. For this reason, we think that thyroid blood flow should be evaluated diurnally by power Doppler in TSH dependent thyroid pathologies, autoimmune diseases affecting TSH receptor, or thyroid nodules considered to develop independently from TSH.