

Morning versus Bedtime Levothyroxine Administration: What is the Choice of Children?

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Introduction and objectives: The present study compared the administration of levothyroxine (LT4) before breakfast and bedtime in school children diagnosed with hypothyroidism and analyzed the effects of timing on thyroid functioning and patient satisfaction.

Methods: A total of 163 children with acquired hypothyroidism (125 females and 38 males) between 8 and 18 years of age and taking LT4 for at least three months were enrolled in the study. The timing of administration of the drug of all subjects was shifted to bedtime. The levels of thyroid hormone and blood lipid, anthropometric measurements, Pediatric Quality of Life Inventory, Morisky Medication Adherence Scale, and Hypothyroidism Symptoms scores were analyzed and compared at the beginning of the study and three months later after the shift in the timing of drug administration.

Results: There was no difference between the bedtime and morning regimens of LT4 with respect to thyroid hormone levels, quality of life, drug adherence, and symptoms of hypothyroidism. At the end of the study, 45 of 70 new-onset treated subjects preferred the bedtime regimen. Also, drug adherence was found to be better in these patients.

Table 1. Characteristics of Patients

	<i>n: 163</i>
Age (y)	13.7 ±2.7
Male Gender (%)	38 (23.3)
Mean Dose (mcg/kg/day)	1.8 ±0.8
Etiology of Hypothyroidism	
Hashimoto Thyroiditis (%)	154 (93.5)
Thyroidectomy (%)	5 (3.2)
Radioactive Iodine Therapy (%)	4 (3.2)
Beginning time of treatment	
3-6 months ago (%)	70 (42.3)
More than one year ago (%)	93 (57.7)

Table 3. Clinical and laboratory findings of the new-onset treated children who preferred bed-time drug administration.

	Morning Time	Bed Time
<i>N: 45</i>		
FT ₄ * (ng/dl)	1.27±0.4	1.29±0.4
FT ₃ * (ng/dl)	3.12±0.8	2.98±0.7
TSH* (uIU/ml)	2.8±1.2	2.4±1.5
Thyroglobulin* (ng/ml)	18.7±14.2	16.7±15.8
Morisky [†]	5.6±0.8	6.9±0.7
PEDSQL*	93.14±7.8	94.21±6.7
Symptom Score*	1.4±0.5	1.2±0.4

FT₄, free thyroxine; FT₃, free triiodothyronine; TSH, thyroid stimulating hormone; PEDSQL, Pediatric Quality of Life Inventory. Data are presented as mean ± SD.

*: Statistically there is no significant difference.

[†]: p<0.05

Table 2. The reasons for the preferred time of drug intake in new-onset treated patients.

Morning time (n: 25)	
Willingness to eat snacks just before sleeping (%)	9 (40.1)
Forgetting drug intake due to suddenly falling asleep at nights (%)	6 (27.3)
Difficulty in falling asleep (%)	4 (18.1)
No reason (%)	5 (22.7)
Bed Time (n: 45)	
Unwillingness to wait for breakfast after drug intake (%)	26 (57.1)
Forgetting drug intake in mornings due to sleepy feeling (%)	7 (17.1)
Forgetting drug intake in mornings due to limitation of time (%)	6 (14.2)
No reason (%)	5 (11.4)

Conclusion: We found no difference between the bedtime and morning regimens in both new-onset and long-standing treated patients. In naive patients, consideration of patient's preference for timing of drug administration may increase their adherence to medication. Therefore, we suggest that choice of drug administration timing should be based on the preference of patients.

1. Geer M, Potter DM, Ulrich H. Alternative schedules of levothyroxine administration. Am J Health Syst Pharm. 2015 Mar 1;72(5):373-7.

2. Bolk N, Visser TJ, Nijman J, Jongste IJ, Tijssen JG, Berghout A. Effects of evening vs morning levothyroxine intake: a randomized double-blind crossover trial. Arch Intern Med. 2010 Dec 13;170(22):1996-2003.