Levothyroxine poisoning in children – should we really be afraid?

Çocukluk çağında levotiroksin zehirlenmesi – gerçekten korkmalı mıyız?

Betul Ozturk[1], Ilknur Bodur[2], Aysun Tekeli[3], Ali Gungor[1], Raziye Merve Yaradilmis[1], Muhammed Mustafa Guneylioglu[1], Aytac Goktug[4], Can Demir Karacan[5], Nilden Tuygun[1]

[1] Department of Pediatric Emergency, Ankara Etlik City Hospital
[2] Department of Pediatric Emergency, University of Health Sciences, Dr Sami Ulus Maternity and Children's Education and Research Hospital
[3] Department of Pediatric Emergency, Gulhane Training and Research Hospital
[4] Department of Pediatric Emergency Istanbul Medeniyet Universitesi Goztepe Egitim Arastirma Hastanesi
[5] Department of Pediatric Emergency Care, Ankara Bilkent City Hospital

Abstract

Aim: L-thyroxine intoxication is rarely seen in children; however, it can be worrying for clinicians and parents. This study aimed to present the clinical and laboratory findings of children admitted to the pediatric emergency department with l-thyroxine intoxication.

Methods: Patients admitted to the pediatric emergency department with l-thyroxine intake between January 2015 and June 2022 were included in this retrospective study. The patient's clinical characteristics, laboratory findings, treatment, and hospital costs were recorded and analyzed.

Results: This study included 33 pediatric patients with thyroxine intoxication. The median age was 35 months (The interquartile range (IQR) 25-47.5) and 19 of them were girls (57,5%). No patient had a clinical symptom at the admittance. One patient had massive l-thyroxine intake and two patients had tachycardia. Gastric lavage and activated charcoal were used in 18 patients. Four patients were followed in the pediatric intensive care unit and one of them was treated with propranolol. The median time of hospital stay was 24 hours (IQR 13,5-84). The median cost of the treatment was United States dollars (IQR56.2-116.75).

Conclusion: L-thyroxine intoxication usually occurs with low drug doses in children and has a benign prognosis. Routine hospitalization of these patients, particularly with low drug dose intake, should be questioned considering the treatment cost.

Keywords: Children; intoxication; l-thyroxin; poisoning; toxicity

Öz

Amaç: L-tiroksin zehirlenmesi çocukluk çağında az görülmesine rağmen, aileler ve klinisyenler açısından endişe verici bir durumdur. Bu çalışmada l-tiroksin zehirlenmesi ile acil servise başvuran çocukların klinik ve laboratuvar bulgularının sunulması amaçlanmıştır.

Yöntemler: L-tiroksin alımıyla Ocak 2015 – Haziran 2022 arası çocuk acil servisine başvuran hastalar geriye dönük olarak çalışmaya dahil edildi. Hastaların klinik özellikleri, laboratuvar bulguları, tedavi ve hastane masrafları kayıt ve analiz edildi.

Bulgular: Bu çalışmada tiroksin intoksikasyonu olan 33 hasta vardı. Hastaların medyan yaşı 35 ay (Interquartil Range (IQR): 25-47.5) ve hastaların 19'u kızdı (57,5%). Başvuru sırasında hiçbir hastada klinik semptom yoktu. Bir hastada masif l-tiroksin alımı varken iki hastada taşikardi mevcuttu. 18 hastada gastrik lavaj ve aktif kömür kullanıldı. 4 hasta çocuk yoğun bakımda takip edildi ve bir tanesi için propranolol tedavisi uygulandı. Ortanca hastanede kalış süresi 24 (IQR 13,5-84) saatti. Ortanca tedavi masrafı ise $73'dı (IQR56.2-116.75).

Sonuç: L-tiroksin zehirlenmesi çocuklarda sıklıkla düşük dozlarda olur ve iyi seyirlidir. Bu hastaların özellikle düşük doz alımı olanların rutin olarak hastaneye yatışı tedavi masrafları göz önüne alındığında yeniden sorgulanmalıdır.

Anahtar Sözcükler: Çocuklar; intoksikasyon; l-tiroksin; toksisite; zehirlenme

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Corresponding author/*Yazışma yazarı*
Betül Öztürk
Ankara Etlik Şehir Hastanesi Çocuk Acil Kliniği, Varlık Mah, Halil Sezai Erkut Cd. No:5, 06170 Yenimahalle/Ankara
E-mail: drbetulozaydinozturk@gmail.com

ORCID
Betül Öztürk: 0000-0002-8000-3599
İlknur Bodur: 0000-0002-4135-5700
Aysun Tekeli: 0000-0002-3639-2224
Ali Güngör: 0000-0003-4139-3480
R. Merve Yaradılmış: 0000-0003-1202-8564
M. M. Güneylioğlu: 0000-0002-9260-6776
Aytaç Göktuğ: 0000-0002-0242-2368
Can Demir Karacan: 0000-0001-5301-8106
Nilden Tuygun: 0000-0002-5359-4215

INTRODUCTION

Unintentional drug poisoning is one of the major causes of morbidity and mortality in children. The most common medications that cause intoxication are antibiotics, antidepressants, and non-steroidal anti-inflammatory drugs (1). Although l-thyroxine intoxication is rare, it can be quite worrying for both clinicians and parents. L-thyroxine poisoning usually occurs accidentally or in a suicide attempt. The toxic dose of l-thyroxine is 3mg/day in children (2). Patients with l-thyroxine poisoning can be asymptomatic and may present with fever, tachycardia, hypertension, tremors, sleeplessness, and anger, particularly in patients exposed to overdose (3). Although rarely seen, patients may also present with more severe symptoms such as coma, convulsion, acute psychosis, and myocardial infarction (4).

The beginning of the symptoms after exposure can be quite varying, as it can prolong to 3 to 11 days, and it is independent of the exposed dose of l-thyroxine (5). Therefore, there is no consensus on the clinical follow-up of patients with l-thyroxine intoxication.

This study aimed to present the demographic and clinical findings of patients admitted to the pediatric emergency department with acute l-thyroxine poisoning and to review the management strategies of these patients.

MATERIAL AND METHODS

This study was conducted in Ankara Dr. Sami Ulus Gynecology, Child Health, and Diseases Training and Research Hospital. This study was approved by Clinical Research Ethics Committee of the University of Health Sciences Dr Sami Ulus Training and Research Hospital ((Date: 02.12.2020, Decision No: 2020-051). Patients who were admitted to the pediatric emergency department with the diagnosis of 'accidental poisoning' (International Classification of Diseases (ICD): X44) between January 2015 and August 2022 and aged 1 month to 18 years were retrospectively evaluated. Only l-thyroxine poisoning patients were included in this study. Patients with multiple drug poisoning were excluded due to the possible drug interactions and mixed patient symptoms.

Patients' age, gender, cause of poisoning (accidental, suicidal), dosage, duration between drug intake and pediatric emergency visit, clinical findings, laboratory findings, treatment, time of hospital stay, and average hospital cost were all recorded.

Statistical analyses

Statistical analysis of the data obtained in the study was made in Statistical Package for the Social Sciences package program version 22.0 (SPSS Inc., Chicago, IL, USA). Software package program. Descriptive statistics [percentage, mean, median, standard deviation (SD), the interquartile range (IQR) were used to define the population included in the study. Parametric data are presented as mean ± SD and nonparametric data as median (IQR).

RESULTS

There were 1890 patients admitted to the pediatric emergency department between January 2015 and August 2022 with the diagnosis of ICD-X44. Of these patients, 35 were l-thyroxine poisoning. Two patients were excluded due to multiple drug intakes. Finally, there were 33 patients with l-thyroxine poisoning. The median age of patients was 35 months (IQR 25-47.5). There were 19 girls (57.5%) and 14 boys (42,5%). While 31 patients (93.9%) unintentionally took the drug, two of them (5.7%) intended suicide. Eight of the patients had been diagnosed with congenital hypothyroidism and all the patients had acute poisoning. The median duration of hospital admittance was 90 minutes (IQR 49-180). None of the patients had clinical symptoms. While one patient (3%) took the drug at a toxic level, the dose of the remaining patients was below the toxic dose of 3gr/dl/day. The median amount of L thyroxin intake was 33 mcg/kg (IQR 20-79,5). The median vital findings were as follows; body temperature 36.4 ±0.54°C, heart rate 115.5 ±17,3 /min, systolic blood pressure 100 ±10 mmHg, and diastolic blood pressure 61 ±15,8 mmHg. Tachycardia was observed in 2 patients (6%). Gastric lavage with activated charcoal was performed in 18 patients (54,5%). Patients' initial laboratory findings are presented in Table 1. Of the 33 patients 12 (36,3%) were treated in the emergency department, 17 (52,5%) were hospitalized and treated in general pediatrics and 4 (11,2%) were treated in the pediatric intensive care unit (PICU). One of four

Table 1. Main findings of the study population

Patients (n=33)	**n (%)**
Age (month, median, IQR)	35 (25-47.5)
Gender	
Girl	19 (57,5)
Boy	14 (52,5)
Duration from drug intake to emergency visit (minutes, median, IQR)	90 (49-180)
Symptoms	
Asymptomatic	33 (100)
Findings	
Tachycardia	2 (6)
Thyroxin dose - median (mcg/kg, IQR)	33 (20-79.5).
Laboratory findings (median, IQR)	
WBC ($x10^3/\mu l$)	10.360 (8050-12765)
Hgb (g/dl)	12,1 (11,6-12,9)
PLT($x10^3/\mu l$)	382000 (281000-466000)
AST (U/L)	34,5 (29,25-42,25)
ALT (U/L)	19,5 (14,25-29,5)
Bun (mg/dL)	13 (10,5-16,5)
Cre (mg/dL)	0,46 (0,44-0,50)
TSH (μIU/mL)	2,7 (1,5-4,7)
fT4 (ng/dL)	1,9 (1,33-3,1)
fT3 (pg/mL)	4,64 (4,4-5,04)

*n: number, IQR: The Interquartile range, WBC: White Blood Cell, Hgb: Hemoglobin, PLT: platelet, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, BUN: Blood, Urea Nitrogen, CRE: Creatine, TSH: Thyroid Stimulating Hormone, fT4: Free Thyroxine, fT3:Free Triiodothyronine

patients in the PICU was treated with intravenous propranolol. The median time of hospital stay was 24 (IQR 13,5-84) hours.

Twenty-two (66.6%) patients had come for a follow-up examination. The median time for a follow-up visit was 3 (IQR 2-6) days. None of the patients developed any symptoms in this period and all the control vital findings were normal. The medial thyroid function tests were as; Thyroid Stimulating Hormone (TSH) 1,38 μIU/mL (IQR 0,36-2,72), thyroxine (fT4) 1,44 ng/dL (IQR 1,22-1,72), triiodothyronine (fT3) 3.72 pg/mL (IQR 3.47-4.52). The median hospital cost for each patient was 73 United States dollars (IQR 56,2-116,75).

DISCUSSION AND CONCLUSION

Levothyroxine intoxication is more common in children than adults but has a better prognosis (6). American Association of Poison Control Center reported 9325 thyroxine intoxication in 2015 and 49% of them were children under 5 years old. Only 0.02% of these children presented with moderate symptoms and there were no deaths (7). Turkish National Poison Advisory Center reported 1460 cases of thyroxine intoxication in 2019 and 52% of these patients were under 6 years old. In addition, %88 patients were reported as asymptomatic and there were no deaths reported (8). The median age and the rate of symptomatic patients in this study were similar to the previous reports.

Litovits and White reported only 4 symptomatic patients with mild fever, anxiety, tachycardia, vomiting, and diarrhea in 78 patients with unintentional levothyroxine intake and they noticed that there were no symptomatic patients if the dose of levothyroxine was under 1.5 milligrams (6). In another study, 41 children under the age of 5 with thyroxine intoxication were evaluated and only 11 children presented with

mild symptoms, and none of them required treatment (9). In two large case series, the thyroxine dose under 4000mcg was reported not to be associated with significant toxicity (10,11). There were only 2 patients with tachycardia in this study; one of them was treated in PICU due to an overdose (over 4 grams), and the other patient's tachycardia was spontaneously resolved.

Gastrointestinal decontamination is the first-line treatment for thyroxine poisoning (12). Most of the patients in this study (54.5%) were initially treated with gastric lavage in the pediatric emergency. Recent studies advise this procedure only in patients with over 5000mcg of thyroxine intake (10,13-15).

The clinical findings of thyrotoxicosis and thyroid storm may occur in normal, low, mild, or high TSH and fT4 concentrations (16). The symptoms and the findings of patients after thyroxine intake are poorly related to the taken dose and the serum fT4 level. Prolonged TSH suppression is anticipated after a high dose of thyroxine intake (17). The TSH and fT4 levels of patients in this study were within the normal limits both at the time of emergency admittance and the follow-up control.

Lewander et al. reported 15 thyroxin intake cases, and they treated most of their patients through outpatient visits and advised routine telemedicine even in patients that took over 4000 mcg of the drug (10). All patients were hospitalized in this study as 17 patients (52,5%) were treated in the general pediatric clinic, 12 (36,3%) in pediatric emergency, and 4 (11,2%) were in PICU. No serious complication was observed in the patients of this study. The mean cost of the treatment in this study was 75 dollars. However, considering the cost of outpatient-based treatment, which is approximately 15 dollars, the results of this study encourage the conservative treatment and telemedicine follow-up of patients with thyroxine intoxication.

The treatment of thyroxine intake should depend on the toxicity level and includes ensuring the airway, controlling sympathomimetic symptoms, controlling body temperature, and the treatment of mental changes. The use of propranolol is only indicated if the patient has significant tachycardia, arrhythmia, and catecholaminergic symptoms, and routine prophylactic use is not recommended (15, 18-20). Propranolol was used in one patient in this study who had taken over 4gr/dl of thyroxine.

The half-life of thyroxine is 48 to 78 hours (13). Majlesi et al. reported a case with tachycardia, tremor, hyperthermia, vomiting, and diarrhea 5 days after 6mg levothyroxine intake and treated the patient with thyrotoxicosis with acetaminophen and propranolol (21). In this study, all patients were asymptomatic at discharge, and we observed no prolonged symptoms in any patient at the follow-up visits.

In conclusion, unintentional acute thyroxine poisoning is usually a benign situation with a low dose intake. Most of the patients are asymptomatic or have mild symptoms. Patients with low drug intake (below 3000 mcg) can be managed through outpatient follow-ups.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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