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Mini Review

Post-Thyroidectomy L-Thyroxine Intoxication: A Mini-Review

Ethem Unal*, Sema Yuksekdag and Abdullah Yildiz

Department of General Surgery, Umraniye Training and Research Hospital, Health Sciences University, Istanbul

***Corresponding Author:** Ethem Unal, Associate Professor of Surgery and Surgical Oncology, Health Sciences University, Istanbul.

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Abstract

Massive L-thyroxine (T4) overdose is usually seen in patients taking replacement treatment after thyroidectomy operations. However, it can be unintentionally ingested by children, or by adults in an attempt to lose weight or for suicidal intentions as well. L-thyroxine intoxication is usually asymptomatic. The most common symptoms are nervousness, insomnia, mild tremor of hands, tachycardia, mild elevation of body temperature, blood pressure elevation and loose stools. However, severe symptoms such as respiratory failure, malignant hyperthermia, seizures, arrhythmia and coma have been reported in the literature. Gastric lavage, activated charcoal, methylprednisolone, cholestyramine and therapeutic plasma exchange are among the treatment options. More important than the treatment protocols, all measures should be undertaken to prevent T4 intoxication especially in patients with a history of thyroidectomy operation.

Keywords: *L-thyroxine (T4); Post-Thyroidectomy; Intoxication*

Introduction

L-thyroxine (T4) replacement after thyroidectomy operations is a common clinical setting. The initiation of replacement therapy often overlaps with the transition from inpatient to outpatient care and it either begun or continued by surgeons, internists, endocrinologists or primary physicians. Thyroid hormone is usually advised to be taken in fasting state with) after 30 to 60 minutes before breakfast. When T4 is taken orally, up to 80 - 90% of it is absorbed, and the peak serum concentration is reached 2 - 4 hours after ingestion [1]. The half-life of T4 is relatively long (7 days) [1,2]. T4 is peripherally converted to its active form, triiodothyronine T3, which has a relatively shorter half-life (one day). In the present study, we reviewed and summarized the present English-written literature in brief.

Discussion

T4 overdose is usually seen in patients taking replacement treatment after thyroidectomy operations. In estimating the required quantity of L-thyroxine replacement in status post-thyroidectomy, one should know the patient's physiological requirement for T4. The patient's age, weight, pregnancy status, medications and diseases that either increase the requirement for L-thyroxine or affect its absorption are among the factors affecting its serum level. As the T4 requirement varies considerably from one person to another, frequent blood tests (T3, T4 and thyroid stimulating hormone-TSH) are mandatory in early postoperative period (in every 4 to 6 weeks). When the serum level is stabilized and kept in its normal ranges, the follow-up tests are then done in 3 to 6 months and in some cases, once a year. In these clinical settings, intoxication can be seen and the patient should be warned against the frequent symptoms seen in case of toxication. In peripheral tissues, T4 is partially converted to T3, a more biologically active thyroid hormone [3]. Since T4 is pharmacologically inactive, T3 is responsible for development of toxicological symptoms [2]. It is clear that if any symptoms appear, they are delayed in onset. Reason for this is that levothyroxine must achieve peripheral conversion to T3.

The majority of previously reported studies report mild symptoms as tachycardia, fever, irritability, hyperactivity, diarrhoea, abdominal pain and hypertension (Table 1) [2,3]. Rarely, massive thyroid hormone overdose has led to grand mal seizures, thyroid storm and even coma, particularly in adults [4]. Overall, previous reports suggest that there is no dose-response relationship between the occurrence or severity of symptoms and amount L-thyroxine ingested [2,5]. Even patients with a relatively low dose of T4 potentially develop seizures and it is not possible to predict which patients will become symptomatic.

General
Fatigue, increased appetite, heat intolerance, fever, weight loss, excessive sweating
Central Nervous System
Headache, nervousness, anxiety, hyperactivity, irritability, emotional lability, insomnia, psychosis, seizure, convulsion, coma, pseudotumor cerebri and craniosynostosis in child
Musculoskeletal
Tremor, muscle weakness, arthralgia, slipped capital femoral epiphysis and premature closure of the epiphyses in child
Cardiovascular
Palpitations, tachycardia, arrhythmia, increased pulse and blood pressure, heart failure, angina pectoris, myocardial infarction, cardiac arrest
Respiratory
Dyspnea, wheezing, respiratory failure
Gastrointestinal
Vomiting, diarrhea, abdominal cramps and elevations in liver function tests
Dermatological
Hair loss, flushing, urticaria, pruritus, skin rash, angioedema
Endocrine
Decreased bone mineral density, osteoporosis, thyroid storm
Reproductive
Menstrual irregularities, impaired fertility

Table 1: *Symptoms and signs seen in L-thyroxine intoxication.*

Therapeutic recommendations are made based only in the review of the available literature concerning a relatively large number of patients, most of them children. In clinical setting, in patients with total thyroidectomy taking T4 replacement therapy, clinical suspicion is important. Cessation of replacement treatment for a while can be sufficient to control early symptoms and clinically overt signs. Acute massive doses of L-thyroxine typically have a mild clinical course that can be controlled by activated charcoal, or possibly cholestyramine, propranolol, dexamethasone, and supporting measures, with close medical evaluation (Table 2). Administration of activated charcoal to stimulate decontamination and prophylactic administration of propranolol (potent beta-adrenergic blocker) to control tachycardia and hypertension should be recommended as the initial treatment [6]. It is well known that propranolol has an effect on decreasing plasma T3 and effect on increasing plasma rT3 in a dose-dependent manner. Other treatments such as propylthiouracil, steroids, iopanoic acid, cholestyramine, sodium iodate and hemoperfusion lacks in evidence [5,6]. In acute intoxication cases, monitoring of vital signs and laboratory data is most important.

Cessation of T4 replacement treatment and close follow-up
Gastric lavage (within hours of ingestion).
Emetic agents
Propranolol (10 - 40 mg 3 times daily)
Activated Charcoal (1 g/kg per oral)
Dexamethasone (decrease the conversion of T4 to T3, 4 mg per oral daily)
Sodium ipodate, if available
Cholestyramine (ion-exchange resin,4g every 8h per oral)
Propylthiouracil (PTU) (can inhibit conversion of T4 to T3)
Activated charcoal hemoperfusion
Plasmapheresis (rarely necessary)
Hemodialysis (probably of limited value)
Thyroid storm: demands treatment in an Intensive Care Unit (ICU)
Phenytoin and phenobarbital (for seizure control)

Table 2: *Treatment options for T4 intoxication.*

Conclusion

Rarely critical cardiac conditions, coma or seizures will follow massive or cumulative doses of T4 [7]. These critical cases and patients in thyroid storm demand treatment in an ICU. Hemoperfusion using activated charcoal is a rather complicated procedure but has been reported to be highly effective in decreasing total serum levels [6]. It should be reserved for adult patients with severe intoxication by very large doses of thyroxine and the same applies to plasmapheresis which has been seldom used.

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