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THYROXINE POISONING

Geraldo Medeiros-Neto, MD, Senior Professor of Endocrinology, University of São Paulo Medical School, Brazil

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CLINICAL RECOGNITION

A massive L-Thyroxine (T4) overdose may be accidentally and unintentionally ingested, most commonly by children and adolescents. It may occur intentionally in young and older adults in an attempt to lose weight, with suicidal intentions, or for undeclared purposes. In some localities thyroxine may be obtained at drugstores without prescription (mostly in the generic form). In some reports thyroxine preparations by a pharmacist had an erroneous LT4 dosage. Thyroid hormone pills used to treat hypothyroid dogs typically contains a much higher dose of thyroid hormone and if mistakenly taken by humans can lead to thyroxine poisoning.

Ingested thyroxine, which is itself probably of modest physiologic significance, is rapidly partially converted to triiodothyronine (T3), the active form of thyroid hormone. Both thyroxine and triiodothyronine levels in serum rise within 1-2 hours of ingestion. Agents that inhibit T4>T3 conversion provide one approach to treatment. In children and adolescents, the clinical course is often very mild. Patients in this age range may ingest a full flask of LT4 with 90-100 tablets (100 or 150 mcg/tablet). Rarely, the overdose is discovered immediately and the patient is brought to the hospital 6-12 hours after the ingestion. At this time, the common clinical signs and symptoms include nervousness, insomnia, mild tremor of hands, tachycardia, mild elevation of body temperature, blood pressure elevation, and loose stools. Rarely more serious late effects occur, including coma, convulsions, and acute psychosis. Cardiac effects aside from tachycardia are seldom seen in young adults but may occur in middle age and older adults, with reported arrhythmias and acute myocardial infarction. However, only one fatality has been reported. Interestingly the onset of symptoms and signs (Table 1) may be delayed for up to 3 to 10 days and does not correlate closely with plasma levels of serum total T4 and total T3. Medical consensus has indicated that serious symptoms are less frequent in children even though children usually have higher mean plasma levels of T4 and T3 than adults for the same overdose of LT4 ingested. One-time ingestion of up to 3 mg thyroxine rarely causes symptoms in adult or children. As already mentioned serious complications are not common, but they can appear days after ingestion, and therefore the patients should be closely monitored.

TABLE 1: SYMPTOMS AND SIGNS AFTER INGESTION OF LT4

Severe toxicity is quite rare in children.
Common-effects:
Nervousness
Insomnia
Mild elevation of temperature
Blood pressure elevation
Loose stools
Rare symptoms:
Comma
Convulsions
Acute psychosis
Thyroid storm
Tachycardia, arrhythmias

DIAGNOSIS and DIFFERENTIAL

Elevated levels of total and free T4 and T3 have been described with suppressed serum TSH levels and otherwise typically a normal biochemical profile (Table 2). The half-life of serum T4 may be shortened. In one study the half-life of LT4 was 5.7 days which is slightly shorter than the usual half-life of L-thyroxine. In one report total serum T3 levels reached the normal range five days after ingestion of 9.9 mg of LT4 (99 tablets of 100 mcg), although free T4 levels were still elevated. In many cases, there is a progressive rise in both serum total T4 and total T3 levels in the first 24 hours following the overdose, caused by continued absorption of the ingested LT4.

Table 2: Biochemical Changes After Ingestion of LT4
Elevated serum total T4 and T3
Suppressed serum TSH
Elevated Free T4 and Free T3
Normal biochemical profile

THERAPY

Therapeutic recommendations are made based only in the review of the available literature concerning a relatively large number of patients, most of them children. Acute levothyroxine overdose is much more common in children compared to adolescents and adults. Therapeutic options are related to the time elapsed after the ingestion of a large number of tablets of L-thyroxine and the actual beginning of emergency therapy (Table 3). 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. Rarely critical cardiac conditions, coma, seizures will follow massive doses of L-Thyroxine.

If more than a few hours of ingestion of LT-4 tablets have elapsed, most probably the tablets have travelled from the gastric cavity to duodenum. Moreover, gastric lavage is difficult to conduct in small children. One way to confirm the presence of LT-4 tablets in the gastric cavity is endoscopy, easily conducted in many hospitals and emergency rooms. LT-4 tablets are dissolved by the gastric juice, but there are no data about the rate of dissolution of a large number of tablets of LT-4. Most probably LT-4 would not be entirely dissolved by the gastric juice and may not be absorbed in the duodenum (normally about 10-15%) but would be absorbed in the jejuno-ileum (normally about 53% of absorption of LT4).

Emetics both local (Ipecac) or central agents (apomorphine) should be avoided.

Administration of activated charcoal is a common practice in many drug overdoses and is an agent that can prevent absorption of several drugs from the gastro-intestinal system. However, in many reports repeated doses of activated charcoal were ineffective in accelerating the elimination of levothyroxine, probably due to high uptake in the duodenum and jejuno-ileum.

Hemoperfusion using activated charcoal is a rather complicated procedure but has been reported to be highly effective in decreasing total serum levels. 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.

Cholestyramine, an ion-exchange resin (Questran ®), can be administered in the usual dose of 4 grams every 8 hours orally. This drug binds thyroxine and enhances its elimination.

Glucocorticoids (Dexamethasone 4 mg orally) decrease the conversion of LT4 to T3, the active hormone. Sodium Ipodate (oral cholecystographic agent) has also been used for blocking the conversion of LT4 to T3, but it is no longer generally available.

Beta-blockers such as propranolol, are useful to ameliorate the metabolic effects of thyroid hormone, mostly on the cardiac system (controlling tachycardia, preventing arrhythmias). Seizures may be treated with phenytoin and phenobarbital. Propylthiouracil (PTU) might be used for blocking the conversion of T4 to T3 but may have very limited usefulness in the presence of a large load of LT4.

Hemodialysis has been used in severe cases, but it is probably of limited value since both T3 and T4 are highly protein-bound.

TABLE 3: TREATMENT OF INGESTION OF A MASSIVE DOSE OF L-THYROXINE

Gastric lavage (within hours of ingestion). Emetic agents (<u>not advised</u>) Propranolol (10-40 mg 3 times daily) Activated Charcoal (1g/kg p.o.) Dexamethasone (4 mg p.o. daily) Sodium ipodate, if available Cholestyramine (4g every 8h p.o.) Propylthiouracil (PTU) (May inhibit conversion of T4>T3) Activated charcoal hemoperfusion Plasmapheresis (seldom necessary) Hemodialysis (probably of limited value) Thyroid storm: demands treatment in an Intensive Care Unit.

FOLLOW-UP

Patients should be monitored for several days to be sure that serum T4 and T3 levels are falling

GUIDELINES

None applicable.

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