



Massive Thyroid Hormone Overdose: Kinetics, Clinical Manifestations and Management

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Key words: thyroid hormone, pharmacokinetics, overdose, activated charcoal, beta-blockers

IMAJ 2002;4:298–299

Hypothyroidism is one of the commonest endocrine disorders, and many prescriptions for thyroid hormone replacement are written yearly. In spite of the extensive availability of this medication, we have observed few cases of large overdoses with thyroid hormone in our hospital from among the 2,000 patients referred for evaluation and treatment of drug overdoses in the past 4 years. We report a massive thyroid hormone overdose in a 13 year old boy.

Patient Description

A 13 year old boy presented to the emergency department after intentional ingestion of 9.9 mg of levothyroxine (99 tablets of 100 µg) 19 hours prior to admission. He was known to have primary hypothyroidism from the age of 6 years and had been on thyroid hormone replacement ever since (100 µg daily).

On admission the patient was in good

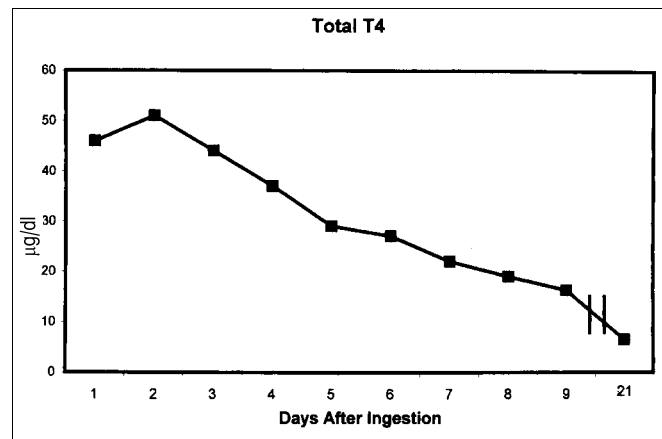
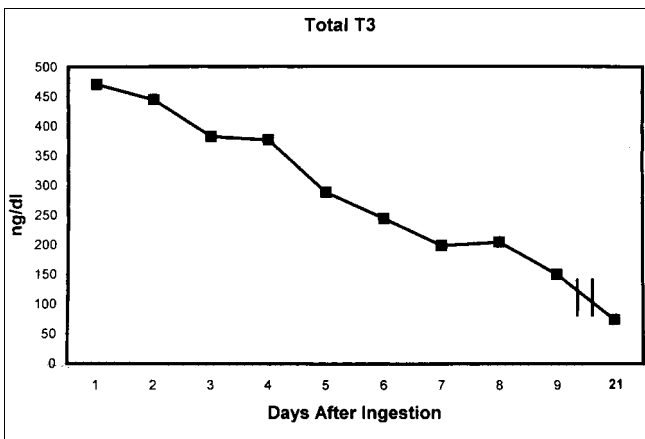
general condition. Blood pressure was 124/68 mmHg, pulse rate 84/min and temperature 37°C. The only positive finding was a mild tremor of the hands. Routine laboratory studies and thyroid function tests were obtained. He was immediately treated with activated charcoal, 1 g/kg per os, propranolol, 10 mg three times daily, and dexamethasone 4 mg daily. The results of routine laboratory tests including complete blood count and automated chemistry battery were normal, except for elevation of alkaline phosphatase compatible with his age. Cholesterol levels dropped from 129 mg/dl immediately at admission to 100 mg/dl on the fourth day post-ingestion.

Total thyroxine and total triiodothyronine levels are shown in Figure 1. The initial total T4 and total T3 levels were 46 µg/dl and 468 ng/dl, respectively (normal

T4 4.5–12.5 µg/dl, normal T3 80–180 ng/dl). Total T4 levels rose from 46 to 51 µg/dl and total T3 from 468 to 474 ng/dl in the first 12 hours following admission to the hospital. Twenty-four hours later (43 hours after the overdose), total T3 levels began to decline, with a calculated half-life of 5.3 days. Total T4 levels began to decline on the fourth day following the ingestion, with a calculated half-life of 5.7 days. Thyroid-stimulating hormone levels were undetectable initially and remained suppressed for 10 days following the overdose.

In order to increase the clearance of thyroid hormone, we administered two additional doses of charcoal, 0.5 g/kg, 4 hours apart on the second day following ingestion, but no significant change in the T4 or T3 half-life was noted after the charcoal treatment. Despite the high thyroid hormones levels, the boy remained almost asymptomatic. The only abnormalities were minor temperature elevations

T4 = thyroxine
 T3 = triiodothyronine



Pharmacokinetics of T3 and T4 after overdose

(up to 37.5°C), tremor of the hands and mild anxiety that was reported by the patient, which resolved spontaneously during his hospitalization. His pulse rate ranged between 80 and 96/min, and the absence of tachycardia could be explained by propranolol treatment. He was discharged after 4 days and was followed in the clinic. Thyroid hormone treatment was resumed 2 weeks later when his free thyroxine and TSH levels returned to normal.

Comment

The patient described in this report ingested a massive overdose of levothyroxine, and in spite of very high levels of T4 and T3, his clinical course was very mild.

The effects of acute overdose with various preparations of thyroid hormone have been described in the literature. Serious toxicity is quite rare [1]. Common effects include nervousness, insomnia, mild tremor, tachycardia, mild elevation of body temperature, blood pressure elevation and loose stools [2]. More serious effects have been described, but rarely, including coma, convulsions [3], acute psychosis and myocardial infarction in a young woman [4]. However, no fatalities have been reported after acute thyroid hormone preparation overdose. The onset of symptoms can be delayed for up to 6–11 days and does not correlate with plasma levels of T4, which can help only in verifying the occurrence of the ingestion. Serious symptoms are less frequent in children, despite higher mean T4 and T3 levels than in adults [5]. One-time ingestions of up to 3 mg levothyroxine rarely cause symptoms in adults and young children. Although serious complications are not common they can appear several days later, and the patients therefore should be closely monitored.

TSH = thyroid-stimulating hormone

Chronic ingestion of large amounts of thyroid hormone preparations result more often in more severe symptoms, including angina pectoris, myocardial infarction, myocarditis, ventricular and atrial arrhythmias, high output heart failure, circulatory collapse, left ventricular hypertrophy, thyrotoxicosis and thyroid storm.

In cases described in the past, the half-life of T4 was shortened in cases of overdose. However in the current case the half-life was about 5.7 days, which is slightly shorter than the regular half-life of the drug but longer than that in previously described cases of levothyroxine overdose. Total T3 levels reached the normal range 5 days after ingestion, although free T4 levels were still elevated. This decline is more rapid than that described in similar cases in the past. It is probably the effect of steroid treatment and supports adding steroids to the treatment regimen in levothyroxine overdose. Of interest was the rise of both total T4 and total T3 levels on the first day following the overdose. This was probably caused by continued absorption of the ingested drug. Also of note is the apparently longer than expected half-life of T3. As has been documented previously, the half-life of T4 in euthyroid individuals is 6.5–7 days, and of T3 25 hours. In our patient, the apparently prolonged half-life of T3 may be explained by continued conversion from the large store of T4. Administration of repeated doses of activated charcoal is becoming a common practice in drug overdose and it can prevent reabsorption of several drugs from the gastrointestinal system. Our case also demonstrates that repeated doses of activated charcoal are ineffective in accelerating the elimination of levothyroxine, probably due to high protein binding.

From a review of the literature the following therapeutic recommendations

can be made for acute levothyroxine overdose: gastric emptying in conscious patients, and administration of a single dose of activated charcoal (1 g/kg) together with a cathartic to decrease absorption. In addition, cholestyramine should be administered, which binds thyroxine and enhances its elimination. Other therapeutic modalities include glucocorticoids or sodium ipodate to decrease the conversion of thyroxine to triiodothyronine, beta blockade to ameliorate the metabolic effects of thyroid hormone, administration of diazepam for seizures, and the addition of phenytoin or phenobarbital for recurrent seizures. Only in severe cases (coma, convulsions, cardiac complications, etc.) should more drastic measures be taken such as plasmapheresis or charcoal hemoperfusion, since these treatment modalities can increase elimination of T4 by 30- and fivefold respectively. Hemodialysis is of little value since both T3 and T4 are highly protein bound.

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Money may be the husk of many things, but not the kernel. It brings you food, but not appetite; medicine, but not health; acquaintances, but not friends; servants, but not faithfulness; days of joy, but not peace or happiness.

Henrik Ibsen (1828-1906), Norwegian playwright whose realistic and controversial works revolutionized European theater