CLINICAL VIGNETTE

Thyrotoxicosis from Long-term Use of Redotex, a Fixed-dose Combination Weight-loss Medication

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Case Description

A 46-year-old female presented to endocrinology for low TSH and low free T4. She was experiencing shortness of breath and tachycardia, and had seen a cardiologist who found TSH 0.031 uIU/mL (ref 0.4-4.5) and Free T4 0.24 ng/dL (ref 0.8-1.8). She had no prior history of thyroid disease and had a normal TSH years prior. The patient had a history of obesity and weighed 96 kg two years prior. She followed a ketogenic diet lost weight to 63 kg. One year ago she started a Mexican weight loss supplement called Redotex. This is a fixed-dose combination pill containing tri-iodothyronine (T3) 75 mcg, D-norpseudoephedrine 50 mg, atropine 0.36 mg, diazepam 8 mg, and aloin 16 mg. She was not familiar with the Redotex and claimed it did not help her lose weight. She had a prior history of anxiety but had not sought treatment. She reported shortness of breath, palpitations, and heat intolerance. Vital signs included blood pressure 137/92 mmHg, heart rate 118 bpm, temperature 36.8 degrees Celsius, weight 64 kg, BMI 24 kg/m2. Her exam was notable for tachycardia with a regular rhythm. Thyroid exam was unremarkable and she had no proptosis or tremor. She was diagnosed with thyrotoxicosis factitia from Redotex and advised to taper off of it gradually over eight weeks to avoid benzodiazepine withdrawal. She was advised to see a mental health professional for her chronic anxiety and declined beta blocker. She was seen 4 weeks later and was taking Redotex one tablet three times per week. Her palpitations had improved, and her heat intolerance had resolved. Her mood initially worsened, but substantially improved. She still had not obtained treatment for anxiety. Seven weeks after the initial presentation, she returned after completely stopping the medication due to experiencing migraines. Her tachycardia had resolved, but her mood had worsened. She had gained 3 kg since the initial presentation. Repeat labs included TSH 3 uIU, Free T4 was 1.2 ng/dL, total T3 was 91 ng/dL (ref 85 – 185). Her DXA was normal.

Discussion

Redotex is a once daily Mexican prescription diet pill, which contains a fixed-dose of five active ingredients: T3 75 mcg, D-norpseudoephedrine 50 mg, atropine 0.36 mg, diazepam 8 mg, and aloin 16 mg. It entered the Mexican market in 1956. Although illegal in the United States, it became popular in the 1980s in Americans who obtained it in Mexico and brought it across the border. Several short-term studies have shown Redotex to be safe and effective, however long-term studies are lacking.[1-3] Three case reports of thyrotoxicosis secondary to brief use (one day to six weeks) have been published.[4,5] We present the first case report of thyrotoxicosis from long-term (one year) use of Redotex. We also review previous literature and real-world safety concerns.

Redotex contains a large dose of T3, which causes iatrogenic thyrotoxicosis in previously euthyroid patients taking the medication for weight loss. For reference, 75 mcg of T3 in Redotex is approximately 15 times the usual (optional) dose of T3 given to patients with hypothyroidism as an adjunct to levothyroxine. A hypothyroid person weighing 64 kg would require 100 mcg of T4, which is roughly equivalent to 25 mcg of T3. Thyrotoxicosis, including T3 toxicosis, commonly causes tachycardia, hypertension, weight loss, tremors, insomnia, frequent bowel movements, anxiety, and heat intolerance. Serious adverse effects include atrial fibrillation, heart failure, stroke, psychosis, and fractures.[6]

Another ingredient of Redotex is D-norpseudophedrine 50 mg, also known as cathine, a psychostimulant introduced in the 1970s for weight reduction.[7] The 30 mg dose was commonly used in Mexico as an over-the-counter nasal decongestant. It is a phenethylamine derivative, structurally similar to amphetamine, diethylpropion, phentermine, and bupropion. These drugs stimulate the release of norepinephrine, serotonin, and dopamine via uptake inhibition. D-norpseudoephedrine is 10 times less potent than amphetamine, with less potential for abuse. It exerts central effects (e.g., anorexia, alertness, increased sensory stimulation, and hyperthermia) as well as peripheral effects (e.g., increased heart rate, respiratory rate, and blood pressure, constipation, and urinary retention). A multicenter, double-blind, randomized, placebo-controlled study of 241 obese patients demonstrated the safety and efficacy of cathine 53.3 mg over 24 weeks. The most common side effects were tachycardia, high blood pressure, chest pain, restlessness, hot flashes, and dry mouth.[8]

The third ingredient of Redotex, atropine, is an anticholinergic agent that competitively blocks muscarinic receptors. It dries secretions and increases heart rate. Side effects include xerostomia, constipation, blurred vision, dyspepsia, and cognitive impairment.[9]

The fourth ingredient of Redotex is diazepam, a long-acting benzodiazepine that was added as a sedative/hypnotic to counteract the stimulant effects of D-norpseudoephedrine and T3. The manufacturers of Redotex stated in their 2015 study that the purpose of diazepam was to "decrease the anxiety associated with obesity, and consequently the bulimic neurosis with binge eating often present in the obese."[10] Side effects include impairment of psychomotor performance, amnesia, dependence, and rebound anxiety. Withdrawal may lead to seizures, so must be tapered off gradually.[11]

The final component of Redotex is aloin, which is an anthraquinone derived from aloe, added for its laxative properties. Mild adverse effects may include abdominal pain, cramps, and diarrhea. High-dose or long-term use of oral aloe is associated with serious adverse effects, including acute hepatitis from hypersensitivity.[12]

In 1987, a New York Times article detailed the illegal import of Redotex to the United States and publicized patient complications such as "high blood pressure, depression, addiction, psychosis and severe diarrhea."[13] Four deaths occurred among American Redotex users, although the causes of death were unproven. Despite decades of many reported adverse effects of Redotex, a randomized, placebo-controlled trial was not published until 2001.[3] In a double-blinded study of 210 patients, the average weight loss after 6 months was 13.5 kg in the treatment arm compared to 1.5 kg in the placebo arm. Adverse effects were reported as mild, and included dry mouth, hand tremor, anxiety, and irritability.

A prospective observational study in 2014 followed 288 patients with obesity who were given Redotex for 4 months, as well as a 500 kCal diet and a walking regimen of 30 minutes 5 days per week.[2] The average weight loss was 9.7 kg (11% body weight). Systolic and diastolic blood pressure decreased by 1 mmHg and 0.7 mmHg. A major limitation of this study is that adverse events were not reported.

A 2015 study described 609 spontaneous reports of adverse events received in the pharmacovigilance unit of the drug's manufacturer from 2009-2014.[10] Ninety-four percent of the events were classified as mild, five percent as moderate, and only one case as severe (goiter). However, this study is limited by reporting bias with voluntary reports from patients and conflict of interests, adverse events were classified and published by the pharmaceutical company.

A prospective, uncontrolled, open-label study of 3,290 overweight and obese patients was performed in 2018.[1] After six months of treatment with Redotex, body weight decreased by an average of 9 kg. Adverse events were described as mild, the most common of which were dry mouth, anxiety, and headache. However, in 2023, a corrigendum was published stating the author had a conflict of interest as the Medical Director of Productos Medix S.A. de C.V, the maker of Redotex.[14]

There are three case reports of Redotex toxicity, all involving very short-term use (i.e., one day to six weeks). They include patients who presented to the emergency department with thyrotoxicosis who required one to three days of observation and treatment including activated charcoal, a benzodiazepine, and/or a beta blocker.[4,5] This is the first case of long-term use with one year of Redotex. Our patient's signs and symptoms of palpitations, tachycardia, and heat intolerance can be attributed to the effects of T3, D-norpseudoephedrine, and atropine. The diazepam was presumably treating her anxiety, which worsened after stopping the medication. Although a randomized-controlled trial and the prospective uncontrolled studies claim the side effects of Redotex are mild, they do not include the long-term hazards of these ingredients. Chronic thyrotoxicosis causes an increased risk of atrial fibrillation, heart failure, bone loss, and fractures. Furthermore, three of the ingredients, T3, D-norpseudoephedrine, and atropine, consistently cause elevated heart rate. Long-term tachycardia can lead to cardiomyopathy. Furthermore, the psychoactive natures of D-norpseudoephedrine and diazepam may lead to dependence. In addition, benzodiazepine withdrawal can lead to life-threatening seizures. When a patient presents with low TSH and low Free T4, both central hypothyroidism and T3 ingestion need to be considered. Taking a thorough history of supplement use and researching their ingredients are critical since patients may be unknowingly taking T3.

In May of 2023, Mexico's health authority officially banned Redotex stating there were 837 reports of adverse reactions. The news article announcing this noted that the combinations of ingredients can cause thyroid dysfunction, stroke, cardiac arrhythmia, seizures, insomnia, pulmonary hypertension, and muscle weakness.[15] The long history of approval despite its dangers is being investigated as a form of corruption among public officials.

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