Teachable Moment

Tirzepatide-Induced Rapid Weight Loss–Related Thyrotoxicosis

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Story From the Front Lines

A 62-year-old male patient with obesity, hypothyroidism, and type 1 diabetes, with a body mass index of 31.2 (calculated as weight in kilograms divided by height in meters squared), and weight of 93 kg presented to the emergency department with palpitations, excessive sweating, confusion, fever, and hand tremors. The results of an electrocardiogram showed atrial fibrillation, and the patient received immediate treatment. Medical history included autoimmune hypothyroidism, obesity, and type 1 diabetes, which had been treated with 200-µg levothyroxine daily, 10-mg tirzepatide weekly, and multiple daily insulin injections, respectively. At presentation, thyrotropin level was 0.001 mIU/L, and free thyroxine level was 7.26 ng/dL. At a recent physician visit 6 months prior, he was prescribed tirzepatide, 2.5 mg weekly, for obesity, and the physician suggested increasing the dose every 4 weeks as tolerated and following up in a month. At that visit, his body mass index was 44.4, weight was 132 kg, thyrotropin level was 1.9 mIU/L, and he received 200-µg levothyroxine daily. He missed the follow-up visit because he lives seasonally in different states; however, the tirzepatide dose was increased as suggested every 4 weeks, up to 10 mg. He also continued tirzepatide, 10 mg weekly, while taking 200-µg levothyroxine daily. His weight was reduced by more than 36 kg in 6 months. After further investigation, the origin of atrial fibrillation was determined to be thyrotoxicosis in the context of rapid weight loss from tirzepatide.

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Box. Common Outpatient Medications That Should Be Closely Monitored in Patients With Rapid Weight Loss[a]

Medications With Weight-Based Dosing
- Insulin
- Levothyroxine
- Anticoagulants (dalteparin, enoxaparin, unfractionated heparin, low-molecular-weight heparin)
- Anticonvulsants (carbamazepine, ethosuximide, phenobarbital, phenytoin, valproate)
- Antituberculosis (isoniazid, rifampicin, pyrazinamide, ethambutol)
- Antibiotics (gentamicin, trimethoprim/sulfamethoxazole)
- Antifungals (fluconazole, voriconazole)

Medications With a Narrow Therapeutic Index
- Phenytoin
- Warfarin
- Lithium carbonate
- Digoxin
- Theophylline
- Tacrolimus
- Valproic acid
- Carbamazepine
- Cyclosporine

Medications With Possible Absorption Problems
- Oral contraceptives

[a] This list is not exhaustive.

Teachable Moment

We shared a case of thyrotoxicosis due to excess exogenous levothyroxine intake in a patient whose weight significantly reduced after being treated with tirzepatide for obesity. Tirzepatide, a gastric inhibitory polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) dual agonist, is administered once weekly to treat patients with obesity and/or type 2 diabetes and may achieve similar weight loss results as bariatric surgery.[1] In a recent randomized clinical trial of people without diabetes, 35% of participants who reached 10 mg/week lost more than 25% of their body weight with tirzepatide in 72 weeks.[1]

Notably, the patient described herein received tirzepatide for obesity despite having type 1 diabetes. Obesity has been increasing among people with type 1 diabetes; in the US T1D Exchange Registry, 29% of adults with type 1 diabetes had overweight, and 20% had obesity.[2] Although tirzepatide has not been approved by the US Food and Drug Administration for treating patients with type 1 diabetes, a recent study examined outcomes of tirzepatide in people with obesity and type 1 diabetes. The study showed a more than 10% reduction in body weight in 6 months with various doses, most up to 7.5 mg.[3]

When starting a GLP-1 analogue, starting with the lowest dose is important to minimize gastrointestinal adverse effects, followed by a dose increase as needed. Starting tirzepatide with the lowest dose of 2.5 mg weekly is suggested, followed by increasing the dose every 4 weeks to the next available dose in 2.5 mg increments, as tolerated and clinically necessary, up to 15 mg weekly. The present patient received an increased dose of up to 10 mg in 4 months as suggested and maintained a 10-mg dose for another 2 months. The insulin dose was then decreased gradually to prevent hypoglycemia; however, he continued to receive the same levothyroxine dose.

Levothyroxine replacement for primary hypothyroidism is based on body weight to achieve euthyroid status and is adjusted further based on serum thyrotropin level. Hypothyroidism, pregnancy, and age can all affect the serum thyrotropin goal; thus, the replacement dose may differ.[4]

Iatrogenic thyrotoxicosis may affect the cardiovascular system, especially in older adult patients; among older patients treated with levothyroxine, a thyrotropin level of less than 0.1 mIU/L was associated with a 3-fold increased risk for atrial fibrillation.[5] To prevent thyrotoxicosis, the levothyroxine dose should be reduced in patients with rapid weight loss. Following levothyroxine treatment initiation or dose adjustment, 4 to 6 weeks is the optimal duration to recheck thyrotropin level and adjust the dose as needed.[4] Although yearly follow-up is adequate, pregnant patients or those with rapid weight loss may require more frequent follow-up visits for dose adjustments.[4] Accordingly, medications with a narrow therapeutic index, those that are

weight-based, and oral contraceptive medications should be carefully monitored with GLP-1 or GIP/GLP-1 analogue use (**Box**).

Excess levothyroxine exposure may cause thyrotoxicosis during tirzepatide treatment in patients who lose a significant amount of weight rapidly. With the increasing use of tirzepatide and other GLP-1 analogues for the treatment of patients with obesity, we recommend evaluating patients using tirzepatide closely (every 4 to 6 weeks initially) for assessment of therapy response, adverse events, and possible dose adjustment of other concomitant medications.

ARTICLE INFORMATION

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