Pharmacodynamic Interaction Between Oral Semaglutide and Hydrochlorothiazide Resulting in Reproducible Hypotension: A Case Report

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ABSTRACT

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly prescribed for type 2 diabetes mellitus (T2DM) and obesity, offering improvements in glycaemic control, weight reduction, and cardiovascular outcomes. Although these agents generally lower blood pressure modestly, clinically significant hypotension is rarely reported in either trial or real-world settings. We describe a 65-year-old man with long-standing T2DM, and well-controlled hypertension managed with olmesartan/hydrochlorothiazide who developed persistent dizziness two weeks after starting oral semaglutide 14 mg daily. Home blood-pressure readings averaged 95/60 mm Hg. Discontinuation of semaglutide led to rapid symptom resolution and blood-pressure rebound to 150/80 mm Hg. Upon rechallenge, hypotension recurred, fulfilling dechallenge-rechallenge criteria (Naranjo score = 7, probable). When hydrochlorothiazide was withdrawn but olmesartan and semaglutide were continued, blood pressure stabilized near 130/78 mm Hg and HbA1c improved from 7.4 % to 5.6 %. This reproducible pattern suggests a pharmacodynamic interaction between semaglutide and thiazide diuretics. Given that GLP-1 RAs promote natriuresis and mild diuresis through renal tubular pathways, concurrent diuretic use may potentiate volume depletion and precipitate symptomatic hypotension. Clinicians should monitor blood pressure closely when initiating GLP-1 RA therapy in patients receiving diuretics and adjust antihypertensive therapy as needed.

Keywords: Semaglutide; GLP-1 receptor agonists; Hypotension; Type 2 diabetes mellitus; Antihypertensive therapy; Diuretics.

Bahrain Med Bull 2026; 48 (1): 3029-3032

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