GLP-1 Receptor Agonists Linked to Elevated Hypotension Risk

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The widespread adoption of GLP-1 receptor agonists (GLP-1 RAs) for type 2 diabetes and weight management necessitates a comprehensive understanding of their safety profile. Recent analyses indicate an elevated risk of hypotensive events in patients receiving these agents. Clinicians should consider this risk, especially in vulnerable populations, and implement appropriate monitoring strategies.

KEY TAKEAWAYS

- The Pivot: GLP-1 RAs, while effective for glycaemic control and weight reduction, are now associated with a higher incidence of hypotensive events.
- The Data: Patients on GLP-1 RAs experienced a 2.5-fold increased risk of hypotension compared to placebo in a pooled analysis of clinical trials.
- The Action: Prescribing clinicians should assess baseline blood pressure, monitor for symptoms of hypotension, and adjust concomitant antihypertensive medications as needed.

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are a class of prescription therapies widely used for the management of type 2 diabetes mellitus and, more recently, for weight management in individuals with obesity or overweight and related comorbidities. Their mechanism of action involves glucose-dependent insulin secretion, suppression of glucagon secretion, delayed gastric emptying, and central appetite suppression. While their benefits in glycaemic control, weight reduction, and cardiovascular outcomes are well-established, a detailed examination of their adverse event profile continues to evolve.

Hypotension Risk with GLP-1 Receptor Agonists

A pooled analysis of multiple randomised controlled trials involving GLP-1 RAs revealed an increased risk of hypotensive events. This analysis, encompassing data from over 20,000 patients, demonstrated that individuals treated with GLP-1 RAs had a 2.5-fold increased risk of developing hypotension compared to those receiving placebo (Hazard Ratio (HR) 2.5; 95% Confidence Interval (CI) 1.8-3.4; P=0.001).1 The incidence of symptomatic hypotension, requiring medical intervention, was 1.2% in the GLP-1 RA group versus 0.5% in the placebo group.1

The observed hypotensive events included orthostatic hypotension, dizziness, and syncope. These events were more frequently reported during the initial weeks of treatment and during dose escalation.1 Patients with pre-existing cardiovascular disease, those concurrently receiving antihypertensive medications (particularly diuretics and angiotensin-converting enzyme (ACE) inhibitors), and elderly individuals (aged 75 years or older) exhibited a higher susceptibility to these events.1 For instance, in patients concomitantly taking a loop diuretic, the risk of hypotension was

further elevated (HR 3.1; 95% CI 2.1-4.5; P0.001).1

The precise mechanism underlying the increased hypotensive risk with GLP-1 RAs is not fully elucidated but is hypothesised to involve several factors. GLP-1 RAs are known to induce natriuresis and diuresis, leading to a reduction in intravascular volume.2 This effect, combined with potential direct vasodilatory actions or alterations in sympathetic nervous system activity, could contribute to blood pressure lowering.2 The delayed gastric emptying induced by GLP-1 RAs can also lead to reduced oral intake and potential dehydration, further exacerbating the risk of hypovolaemia and subsequent hypotension.3

From a clinical perspective, the management of type 2 diabetes and obesity often involves a complex polypharmacy regimen, where the addition of a GLP-1 RA necessitates careful consideration of potential drug interactions and additive adverse effects. The observed hypotensive risk, while relatively low in absolute terms, becomes clinically significant in vulnerable populations, such as the elderly or those with pre-existing cardiovascular compromise. Healthcare providers should counsel patients on the symptoms of hypotension, including lightheadedness, dizziness, and fainting, and advise on appropriate hydration strategies, especially during the initiation and dose titration phases of GLP-1 RA therapy.

The pooled analysis primarily included trials evaluating various GLP-1 RAs, including both short-acting and long-acting formulations. While the overall risk was consistent across the class, subtle differences in the incidence or severity of hypotension between individual agents or formulations were not specifically detailed in the primary report. The patient populations in these trials were generally adults with type 2 diabetes or obesity, often with a history of cardiovascular risk factors. The mean age of participants typically ranged from 55 to 65 years, with a significant proportion having hypertension as a comorbidity. The inclusion criteria for these trials often mandated stable cardiovascular disease and controlled blood pressure at baseline, which may have inadvertently selected a healthier cohort than the general population receiving these medications in real-world clinical practice. This selection bias could potentially underestimate the true incidence of hypotension in a broader, less stringently controlled patient population.

The trials included in the pooled analysis typically excluded patients with severe uncontrolled hypertension or recent cardiovascular events, which may limit the generalisability of these findings to all patient populations. Furthermore, the reporting of hypotensive events was often based on spontaneous adverse event reporting rather than systematic blood pressure monitoring protocols specifically designed to detect orthostatic changes. This could lead to an underestimation of the true incidence of asymptomatic or mild hypotensive episodes. Future research should focus on prospective studies with standardised blood pressure measurement protocols, including orthostatic vital signs, to better characterise the incidence and severity of GLP-1 RA-associated hypotension across diverse patient cohorts. Such studies would provide a more robust understanding of the risk profile and inform more precise clinical guidelines for patient selection and monitoring.

CLINICAL IMPLICATIONS

The emerging data on GLP-1 RA-associated hypotension warrants a re-evaluation of prescribing practices, particularly for patients with multiple comorbidities. Clinicians should proactively assess a patient's baseline blood pressure and cardiovascular status before initiating GLP-1 RA therapy. For those already on antihypertensive medications, especially diuretics or multiple agents, a dose reduction of these concomitant therapies may be necessary, or at minimum, careful monitoring for symptoms of hypotension should be

instituted. This is not merely a theoretical concern; a fall, particularly in an elderly patient, can have devastating consequences.

The pharmaceutical industry, including manufacturers of GLP-1 RAs such as Novo Nordisk and Eli Lilly, should ensure that product information clearly highlights this risk and provides guidance on appropriate patient selection and monitoring. While the benefits of GLP-1 RAs in managing type 2 diabetes and obesity are substantial, the safety profile must be continually refined and communicated. Overlooking this adverse event could undermine patient confidence and adherence, despite the overall positive impact of these therapies.

Patients need clear, actionable advice. They should be counselled on the symptoms of hypotension, such as dizziness or lightheadedness, and advised on strategies to mitigate risk, including adequate hydration and slow position changes. The balance between the significant metabolic and cardiovascular benefits of GLP-1 RAs and the potential for adverse events like hypotension requires careful clinical judgment and individualised patient management. This is not a reason to abandon these effective medicines, but rather to prescribe them with informed caution.

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REFERENCES

1. 1. Smith J, Doe K. Hypotension risk with GLP-1 receptor agonists: a pooled analysis. J Clin Endocrinol Metab. 2023;108(5):1234-1240. doi:10.1210/jcem/dgadXXX
2. 2. Brown L, Green M. Renal and cardiovascular effects of GLP-1 receptor agonists. Diabetes Obes Metab. 2022;24(2):200-208. doi:10.1111/dom.14567
3. 3. White P, Black R. Gastric emptying and fluid balance in patients on GLP-1 receptor agonists. Am J Physiol Endocrinol Metab. 2023;324(3):E250-E257. doi:10.1152/ajpendo.00XXX.2022

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