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Review Article

Tirzepatide: A Review Of Its Mechanism Of Action, Clinical Efficacy, And Emerging Importance In Diabetes And Obesity Treatment

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder characterized by insulin resistance, progressive beta-cell dysfunction, and frequent coexistence with obesity, dyslipidemia, and hypertension. Modern treatment aims not only to achieve glycemic control but also to reduce body weight and lower the risk of long-term complications.Tirzepatide is a novel once-weekly injectable medication that acts as a dual agonist of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. This unique dual mechanism enhances glucose-dependent insulin secretion, suppresses glucagon release, delays gastric emptying, and increases satiety, leading to improved blood glucose control and significant weight loss. Because its insulin-stimulating effect is glucose-dependent, tirzepatide carries a lower risk of hypoglycemia when used alone.Clinical evidence from the SURPASS trials has demonstrated that tirzepatide provides greater reductions in HbA1c and body weight than placebo, GLP-1 receptor agonists, and basal insulin. Unlike some insulin therapies, it promotes weight loss rather than weight gain, making it particularly beneficial for patients with T2DM and obesity. Its once-weekly administration may also improve treatment adherence. To minimize gastrointestinal adverse effects such as nausea, vomiting, and diarrhea, therapy is initiated with gradual dose escalation.Overall, tirzepatide represents a major advancement in T2DM management by addressing both glycemic control and obesity. Although long-term cardiovascular and renal outcome data are still emerging, current evidence supports its efficacy, safety, and potential as a comprehensive metabolic therapy.

INTRODUCTION

Type 2 diabetes mellitus is a long-term metabolic disorder in which blood glucose becomes

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persistently elevated because of insulin resistance and progressive loss of pancreatic beta-cell function. Many individuals with T2DM also have obesity, dyslipidemia, hypertension, and elevated cardiovascular risk, so treatment is no longer focused only on lowering glucose. Modern therapy aims to improve glycemic control, reduce body weight, and lower the risk of complications. Tirzepatide has become an important option because it addresses several of these goals at the same time.[1,2,3]Tirzepatide is a novel once-weekly injectable medicine that acts on two incretin receptors, GIP and GLP-1. This dual mechanism makes it different from traditional antidiabetic drugs and even from many newer incretin-based therapies. Clinical studies have shown that tirzepatide can lower HbA1c substantially and also produce notable weight loss, which is particularly valuable in patients with T2DM and obesity.[1,4,5]Interest in tirzepatide increased rapidly after the SURPASS program showed strong glucose-lowering efficacy across different treatment settings. The drug was studied as monotherapy, as add-on therapy, and in comparison with established agents such as semaglutide, dulaglutide, and insulin-based regimens. The overall findings suggested that tirzepatide may represent a new step forward in diabetes management.[4]

Mechanism of action

Tirzepatide is a dual GIP and GLP-1 receptor agonist. GLP-1 receptor activation increases glucose-dependent insulin secretion, lowers glucagon secretion, delays gastric emptying, and promotes satiety. GIP receptor activation also supports insulin secretion and may contribute to better metabolic regulation and energy balance. By combining both actions in one molecule, tirzepatide can influence several pathways involved in diabetes and obesity.[1,2,3]This dual incretin approach is clinically important because T2DM is not only a disease of high glucose but also a disorder of abnormal appetite control, weight gain, and impaired insulin response. Tirzepatide therefore acts at multiple points in the disease process rather than targeting only one abnormality. That broader mechanism may help explain why its effects on HbA1c and body weight are stronger than those seen with some single-pathway therapies.[3,4,6]Another important feature is that tirzepatide stimulates insulin release in a glucose-dependent manner. This means the insulin response is stronger when glucose is elevated and weaker when glucose is normal. As a result, the risk of hypoglycemia is lower when tirzepatide is used alone, although the risk can rise when it is combined with insulin or sulfonylureas.[1,2,5]

Once-weekly dosing

Tirzepatide is given as a subcutaneous injection once weekly. This dosing schedule is easier for many patients than daily injectable treatment. Weekly administration may reduce treatment burden and can be especially useful for people who already take many medicines for diabetes or related conditions.[1,2]

Treatment usually begins with a low dose, followed by gradual dose increases. This stepwise titration is not only for efficacy but also for tolerability. Gastrointestinal side effects are more common when treatment is started or when the dose is raised too quickly, so a slow and structured escalation helps reduce discomfort and improves the likelihood of long-term use.[2,5,10]

The convenience of weekly use is a meaningful practical advantage in real-world care. Patients often prefer fewer injections, and simpler regimens may support better adherence over time. In chronic diseases such as diabetes, adherence is a major factor in treatment success, so once-

weekly dosing may improve both convenience and clinical outcomes .[2,7,15]

Efficacy in HbA1c control

Tirzepatide has shown very strong HbA1c-lowering effects across clinical studies. HbA1c is an important measure of long-term glucose control, and reductions in HbA1c are linked to lower risk of diabetic microvascular complications. In SURPASS-1, tirzepatide produced large HbA1c reductions compared with placebo, and similar improvements were seen throughout the broader SURPASS program.[1,12,13]A major review of clinical studies found that tirzepatide lowered HbA1c in a dose-dependent manner and outperformed placebo, GLP-1 receptor agonists, and basal insulin in many settings. These results are important because they suggest that tirzepatide is not only effective but also among the most potent glucose-lowering therapies currently available for T2DM.[4,5,6] Real-world evidence has also supported these findings. Observational studies show that patients using tirzepatide in routine practice experience meaningful reductions in A1c, often along with improved weight outcomes. This matters because benefits seen in controlled trials are more convincing when they are also reproduced in everyday care.[7,8]

Weight reduction

One of the most clinically important features of tirzepatide is its ability to reduce body weight. Weight loss is highly relevant in T2DM because obesity increases insulin resistance, worsens metabolic control, and contributes to cardiovascular risk. In many patients, even moderate weight reduction can make diabetes easier to manage.[3,4,6]Tirzepatide reduces weight through a combination of appetite suppression, earlier satiety, delayed gastric emptying, and lower food intake. Patients often report that they feel full sooner and eat less overall. This effect is not only cosmetic; it can improve insulin sensitivity, lower blood pressure, and contribute to broader metabolic benefits.[3,6,9] In comparative evidence, tirzepatide has often led to more weight loss than several other diabetes medicines. This is one reason it is particularly attractive for patients with T2DM and overweight or obesity. The drug may therefore help address both hyperglycemia and excess body weight at the same time, which is a major advantage in modern diabetes care .[4,5,8]

Safety profile

Tirzepatide is generally considered to have an acceptable safety profile. The most frequent adverse effects are gastrointestinal, and most are mild to moderate. In clinical trials, serious adverse events were relatively uncommon, and hypoglycemia was not markedly increased when tirzepatide was used without insulin or sulfonylureas.[1,4,5] The main safety concern is tolerability during dose escalation. Nausea, vomiting, and diarrhea can lead some patients to stop treatment early if symptoms are not managed well. For this reason, careful counseling before treatment starts is important. Patients should understand that symptoms are often temporary and may improve with time and gradual titration.[2,5,10]

From a clinical perspective, safety monitoring should include hydration status, gastrointestinal symptoms, and the risk of hypoglycemia if tirzepatide is combined with other glucose-lowering agents. Although the safety profile is favorable overall, treatment success depends on matching the drug to the right patient and using it carefully in combination therapy.[2,5,15]

Common side effects

The most common side effects are nausea, vomiting, diarrhea, constipation, abdominal

discomfort, and reduced appetite. These effects are typical of incretin-based therapies and are usually most noticeable early in treatment or after dose increases. In many patients, symptoms become less frequent as the body adapts.[1,5,9] Nausea is often the leading complaint. It may be mild and manageable, but in some patients it can interfere with eating or daily comfort. Diarrhea and vomiting are also important because they can contribute to dehydration if not addressed promptly. Drinking enough fluids and using slower dose escalation can help reduce these problems.[5,10,11] The reduced appetite associated with tirzepatide is a desired effect in many patients because it supports weight loss. However, when appetite suppression becomes too strong, patients may need dietary advice to maintain adequate nutrition. Therefore, side effects should not only be listed but also actively managed in clinical practice.[2,5,10]

Comparison with other diabetes drugs

Compared with many other glucose-lowering drugs, tirzepatide often provides greater HbA1c reduction and more weight loss. This makes it different from therapies that mainly improve glucose without much effect on body weight. In many studies, tirzepatide outperformed placebo and several active comparators, including GLP-1 receptor agonists and insulin-based regimens.[4,5,12]Compared with basal insulin, tirzepatide may lower weight rather than cause weight gain, which is a major advantage for many patients with T2DM. Compared with some GLP-1 receptor agonists, it may provide stronger glycemic and weight effects. These differences help explain why tirzepatide is being seen as a high-potency treatment option.[4,6,13].The once-weekly route also offers a practical comparison advantage. Daily or more frequent regimens can be difficult for some patients to maintain over time. Tirzepatide's dosing schedule may therefore be more acceptable for people who want effective treatment with fewer injections.[2,7,15]

SURPASS trial evidence

The SURPASS program is the core evidence base for tirzepatide in T2DM. In SURPASS-1, tirzepatide monotherapy improved HbA1c and body weight more than placebo, with no major signal for severe hypoglycemia. This trial helped establish the drug as a strong candidate for diabetes treatment.[12,13] Other SURPASS studies evaluated tirzepatide in patients already receiving basal insulin, other oral agents, or comparators such as dulaglutide and insulin degludec. Across these studies, tirzepatide consistently produced robust glycemic improvement and marked weight loss. This consistency across different treatment settings is one of the most impressive findings in the clinical development program.[4,12,13]

The SURPASS results also showed that the safety profile was manageable and broadly consistent with incretin-based therapy. Gastrointestinal side effects were common, but serious hypoglycemia was uncommon in most settings. Together, these findings helped support the role of tirzepatide as an important treatment option for people with T2DM.[1,4,12]

Long-term perspective

Although current evidence is strong, more long-term data are still needed. Future studies will help clarify the durability of HbA1c lowering, the persistence of weight loss, and the effect on cardiovascular and renal outcomes. These outcomes are especially important because T2DM is a lifelong disease and treatment choices must remain beneficial over many years.[3,6,14] Real-world evidence will also continue to matter. Controlled trials show what a drug can do under study conditions, but routine practice reveals how well it works across diverse patients and

healthcare settings. As more observational data become available, the practical role of tirzepatide in diabetes care will become even clearer.[7,8,15]

Future Directions

Future research on tirzepatide is likely to focus on whether its benefits extend beyond glucose lowering and weight loss into long-term cardiovascular and kidney protection. Reviews and emerging analyses describe tirzepatide as a promising therapy whose future role will depend on more outcome data in large patient groups.[16]

Another important direction is confirming how well tirzepatide performs in everyday clinical practice over longer periods, including adherence, tolerability, and durability of HbA1c and weight reduction. Researchers are also expected to explore its place in people with obesity, prediabetes, and cardiometabolic disease, since current studies suggest broad metabolic potential.[17]

Discussion

Tirzepatide is a dual GIP/GLP-1 receptor agonist that has shown strong effectiveness for improving blood sugar control and promoting weight loss in people with type 2 diabetes and obesity. Long-term data suggest that it can produce sustained reductions in HbA1c and body weight, with benefits extending over extended treatment periods. Compared with semaglutide, tirzepatide appears to produce greater weight loss in available comparative studies, although the evidence still has some limitations and needs further confirmation. Overall, the article evidence supports tirzepatide as a promising option for metabolic disease management, with gastrointestinal side effects remaining the main tolerability concern.[18,19,20]

CONCLUSION

Tirzepatide is a highly effective once-weekly treatment for type 2 diabetes mellitus. Its dual GIP and GLP-1 receptor action gives it strong glucose-lowering power and meaningful weight-loss benefits. The drug has a generally acceptable safety profile, with gastrointestinal side effects being the main limitation.[1,4,5] Because it improves both HbA1c and body weight, tirzepatide is especially useful in patients with T2DM and obesity. The SURPASS studies and real-world reports support its clinical value, while its weekly dosing adds convenience. Overall, tirzepatide represents an important step in the evolution of diabetes therapy.[12]

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