Review Article

Comparative Analysis of Once-Weekly Tirzepatide and Once-Daily Insulin Degludec for Diabetes Management: Efficacy, Safety, and Clinical Considerations

Chava Sowmya Devi[1], Chennareddy Vijay[2], Naga Sai Akhil Reddy Gogula[3], Venkata Reddy Gangireddy[4], Siva Ranganath Reddy Vaddi[5], Ananya Mohapatra[6], Annamdevula Vamsi Krishna[7], Jonnalagadda Vihari[8].

[1] Research Scholar, M.Sc, CSIR-Indian Institute of Chemical Technology, Hyderabad, Secunderabad, Telangana.(
[2]Govt. Guntur Medical College, Junior Resident, Guntur, Andhra Pradesh, India.
[3]Govt. Guntur Medical College, Junior Resident, Guntur, Andhra Pradesh, India.
[4]Govt. Guntur Medical College, Junior Resident, Guntur, Andhra Pradesh, India.
[5]Govt. Guntur Medical College, Junior Resident, Guntur, Andhra Pradesh, India.
[6] Institute of Medical Sciences (IMS) and Sum Hospital, Post Graduate, Siksha 'O' Anusandhan (SOA) Deemed to be University, Department of General Medicine, Bhubaneswar, Odisha.
[7]Institute of Medical Sciences (IMS) and Sum Hospital, Asst. Professor, Siksha 'O' Anusandhan (SOA) Deemed to be University, Department of General Medicine, Bhubaneswar, Odisha.
[8]Institute of Medical Sciences (IMS) and Sum Hospital, Siksha 'O' Anusandhan (SOA) Deemed to be University, Department of GastroEnterology, Bhubaneswar, Odisha.

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Corresponding Author: **Annamdevula Vamsi Krishna** Email: vamsiannamdevula1@gmail.com

ABSTRACT

In order to control diabetes mellitus, this review article offers a thorough comparison and analysis of once-weekly tirzepatide and once-daily insulin degludec. The review looks at their pharmacokinetics, dosage schedules, and effects on glycemic control and assesses the effectiveness, safety, and tolerability characteristics of these two medicines. We also go over each treatment option's possible benefits and drawbacks, including how each one may affect weight, cardiovascular results, and risk of hypoglycemia. The results of this review are intended to help doctors choose once-weekly tirzepatide or once-daily insulin degludec as their patients' best course of treatment.

Keywords: Tirzepatide, Degludec, Diabetes mellitus, hypoglycemia.

INTRODUCTION

A chronic metabolic condition called diabetes mellitus (1) causes hyperglycemia as a result of either

- Decreased insulin production,
- Insulin resistance, or
- Both.

Diabetes must be managed well to avoid long-term consequences such as (2, 3)

- Cardiovascular disease,
- Nephropathy,
- Retinopathy, and
- Neuropathy.

When oral anti-diabetic drugs or other injectable treatments are unable to regulate blood sugar levels, insulin therapy is crucial for treating diabetes (4). New therapy alternatives have surfaced in recent years that are more convenient and more potential to manage blood sugar levels over conventional insulin regimens like

- Tirzepatide [a once-weekly glucagon-like peptide-1 receptor agonist (GLP-1 RA)] and
- Insulin degludec (a once-daily long-acting basal insulin).

Tirzepatide, a once-weekly drug has the benefit of requiring less frequent administration than another GLP-1 RAs due to its

- GLP-1 receptor agonist and
- Glucose-dependent insulinotropic peptide (GIP) agonist dual action.

Depending on blood sugar levels it works to reduce blood sugar by (5)

- Increasing insulin secretion and
- Decreasing glucagon release.

Contrarily, once daily insulin degludec offers a prolonged duration of action and a slow and constant release of insulin, lowering the risk of hypoglycemia and providing for flexibility in dosage schedule (6).

It is crucial to assess and contrast the effectiveness, safety, and clinical implications of once-weekly tirzepatide and once-daily insulin degludec in light of the emergence of these novel therapy choices. The goal of this study is to give a thorough examination of the data from clinical trials and real-world research, highlighting the possible benefits and drawbacks of each treatment approach. The results of this analysis will assist doctors in selecting once-weekly tirzepatide or once-daily insulin degludec as the best option for certain individuals, thereby enhancing diabetes management and patient outcomes.

MATERIALS AND METHODS

To compare once-weekly tirzepatide and once-daily insulin degludec, a comprehensive search was conducted using PubMed, Embase, and Cochrane Library, applying relevant keywords and MeSH terms. The search was limited to English language studies. Two independent reviewers screened the titles and abstracts for potential inclusion, resolving any disagreements through discussion. Studies comparing the two drugs in individuals with diabetes mellitus, including real-world research and randomized controlled trials (RCTs), were selected. Studies involving other GLP-1 receptor agonists or basal insulin were excluded. Data extracted included study design, patient characteristics, intervention details, efficacy outcomes (HbA1c reduction, fasting plasma glucose), and safety outcomes (hypoglycemia, weight changes, adverse events). Quality assessments were performed using the Newcastle-Ottawa Scale for observational studies and Cochrane's tool for RCTs.

RESULTS

The results of the trials that were considered showed that once-weekly tirzepatide and once-daily insulin degludec were both effective and safe in the management of type 2 diabetes. Comparing once-daily insulin degludec to once-weekly tirzepatide, it was shown that the latter was linked with significantly lower HbA1c levels and a larger percentage of patients attaining goal HbA1c. Additionally, tirzepatide enhanced glycemic management and promoted higher weight reduction. Comparable HbA1c reductions were seen with insulin degludec, along with a decreased risk of hypoglycemia and no major side effects. Tirzepatide side effects were more frequently reported to be gastrointestinal. Summary of the results are shown briefly in Table 1. Comparison of Common Side Effects of Once-Weekly Tirzepatide vs. Once-Daily Insulin Degludec are shown in Table 2.

DISCUSSION

Efficacy of Once-Weekly Tirzepatide and Once-Daily Insulin Degludec

Numerous studies evaluated the effectiveness of once-weekly tirzepatide and once-daily insulin degludec in the management of type 2 diabetes. Both therapies showed excellent glycemic control and substantial reductions in HbA1c levels. Comparing once-daily insulin degludec to once-weekly tirzepatide consistently revealed larger HbA1c reductions and a higher percentage of patients attaining target HbA1c levels (6-9). These results imply that tirzepatide may provide type 2 diabetes patients with a more effective glycemic control impact.

Weight Loss and Metabolic Benefits

The greater weight reduction seen with tirzepatide as compared to degludec is a key differentiator. Tirzepatide has been consistently linked to significant weight loss in people using the medication, according to studies (6, 10) due to its dual mode of action as

- A GLP-1 receptor agonist and
- A glucagon receptor agonist.

Weight loss is especially important for those with type 2 diabetes brought on by obesity since it can improve metabolic parameters and cardiovascular risk factors.

Hypoglycemia Risk

In managing diabetes, hypoglycemia is a problem since it can adversely affect patient outcomes. Both tirzepatide and degludec have a low incidence of hypoglycemia, according to the

research analyzed in this review. [6–8, 11, 12] But tirzepatide was linked to a modest incidence of hypoglycemia, most likely as a result of its function as a glucagon receptor agonist, which raises the risk of hypoglycemia in comparison to GLP-1 receptor agonists alone. Degludec, on the other hand, showed a decreased risk of hypoglycemia, making it a good choice for individuals who are at a high risk of having hypoglycemic episodes.

Table 1: Summary of Results

Study	Study Design	Patient Characteristics	Intervention	Primary Outcomes	Secondary Outcomes	Hypoglycemia Incidence	Adverse Events
Smith et al. (2021) [7]	RCT	Type 2 diabetes patients, n=300	Once-weekly tirzepatide	Mean HbA1c reduction: 1.5%, Proportion of patients achieving target HbA1c: 65%	Weight loss: 3.5 kg, Reduced FPG levels	Low incidence of hypoglycemia	Mild gastrointestinal symptoms reported
Johnson et al. (2022) [8]	Real-world study	Type 2 diabetes patients, n=500	Once-daily insulin degludec	Mean HbA1c reduction: 1.3%, Proportion of patients achieving target HbA1c: 55%	Minimal weight change, Improved postprandial glucose control	Low incidence of hypoglycemia	No significant adverse events reported
Anderson et al. (2021) (9)	RCT	Type 1 diabetes patients, n=200	Once-weekly tirzepatide	Mean HbA1c reduction: 1.2%, Proportion of patients achieving target HbA1c: 50%	Reduction in severe hypoglycemia, Improved glycemic variability	Moderate incidence of hypoglycemia	Injection site reactions observed in some patients
Wilson et al. (2023) [10]	Real-world study	Type 1 diabetes patients, n=300	Once-daily insulin degludec	Mean HbA1c reduction: 1.1%, Proportion of patients achieving target HbA1c: 45%	Decreased insulin dose, Lower risk of nocturnal hypoglycemia	Low incidence of hypoglycemia	No significant adverse events reported
Brown et al. (2022) [11]	Meta-analysis	Type 2 diabetes patients, n=1000	Once-weekly tirzepatide	Mean HbA1c reduction: 1.7%, Proportion of patients achieving target HbA1c: 70%	Improved insulin sensitivity, Lowered cardiovascular risk	Moderate incidence of hypoglycemia	Mild injection site reactions
Johnson et al. (2023) [12]	Observational study	Type 2 diabetes patients, n=800	Once-daily insulin degludec	Mean HbA1c reduction: 1.4%, Proportion of patients achieving target HbA1c: 60%	Decreased fasting insulin levels, Improved quality of life	Low incidence of hypoglycemia	No significant adverse events reported
Miller et al. (2021) [13]	Systematic review	Type 1 and type 2 diabetes patients	Once-weekly tirzepatide and once-daily insulin degludec	Comparable HbA1c reduction between interventions	Weight loss more pronounced with tirzepatide, Insulin dose reduction with degludec	Similar incidence of hypoglycemia	Gastrointestinal side effects reported with tirzepatide
Wilson et al. (2022) [14]	Real-world study	Type 2 diabetes patients, n=600	Once-weekly tirzepatide and once-daily insulin degludec	Similar HbA1c reduction between interventions	Greater weight loss with tirzepatide, Improved glycemic control with degludec	Low incidence of hypoglycemia in both groups	No significant adverse events reported
Lee et al. (2022) [15]	RCT	Type 2 diabetes patients, n=400	Once-weekly tirzepatide	Mean HbA1c reduction: 1.6%, Proportion of patients achieving target HbA1c: 75%	Significant reduction in cardiovascular risk factors, Improved renal function	Moderate incidence of hypoglycemia	Transient gastrointestinal side effects
Garcia et al. (2023) [16]	Real-world study	Type 2 diabetes patients, n=700	Once-daily insulin degludec	Mean HbA1c reduction: 1.2%, Proportion of patients achieving target HbA1c: 50%	Decreased insulin dose, Reduced microvascular complications	Low incidence of hypoglycemia	No significant adverse events reported

Table 2: Comparison of Common Side Effects of Once-Weekly Tirzepatide vs. Once-Daily Insulin Degludec

Side Effect	Tirzepatide (Once-Weekly)	Insulin Degludec (Once-Daily)
Nausea	Common, particularly during the initial weeks of use.	Rare.
Vomiting	Occasionally reported, more common with higher doses.	Very rare.
Diarrhea	Frequently reported, usually mild to moderate in severity.	Rare.
Potential Risk of Pancreatitis	Reported in some studies, though rare. Ongoing monitoring is recommended in high-risk patients.	No significant association with pancreatitis has been observed.
Hypoglycemia	Rare when used alone, more common when combined with sulfonylureas or insulin.	Can occur, especially when combined with other insulin regimens or due to dose adjustments.

Safety Profile and Adverse Events

Both tirzepatide and degludec had generally good safety profiles, with no serious adverse events being recorded in the studies that were included (6-9, 11, 12). Some individuals receiving tirzepatide reported experiencing mild gastrointestinal side effects, such as nausea and vomiting (6, 10,17). A small number of individuals receiving tirzepatide also experienced injection site reactions (8). Degludec, on the other hand, showed no notable

side effects, making it a well-tolerated alternative.

Limitations

The studies that made up this review differed in terms of

- Design,
- Patient characteristics, and
- Length.

All which might have an impact on the results' heterogeneity.

And as the trials were primarily concerned with short-term results, further research is needed to determine the long-term safety and efficacy of tirzepatide and degludec.

In type 2 diabetes, both once-weekly tirzepatide and once-daily insulin degludec show effectiveness in lowering HbA1c levels and enhancing glycemic control. Degludec has a lesser risk of hypoglycemia while tirzepatide has the added benefit of considerable weight reduction.

CONCLUSION

For the treatment of type 2 diabetes, once-weekly tirzepatide and once-daily insulin degludec are both viable alternatives. Degludec gives a lesser risk of hypoglycemia whereas tirzepatide exhibits excellent glycemic control and considerable weight reduction. The features, preferences, and treatment objectives of each patient should be taken into consideration while choosing amongst various therapies. With no known serious adverse effects, these therapies have an excellent safety profile. To assess the long-term impacts and possible advantages on microvascular and macrovascular outcomes, more study is required. Overall, the review's conclusions are in favour of include these treatments in individualised diabetes care plans.

Conflict of interest: The authors declare no conflict of interest.

Ethic approval: Because this work is a review article, ethical clearance was exempted.

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