Advances in the Management of Type 2 Diabetes Mellitus

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Diabetes mellitus is a chronic metabolic disorder of the endocrine system, characterized by a complex and varied pathophysiology. Worldwide, there is a dramatic increase in the number of patients with type 2 diabetes, and hence it is becoming a serious threat to the health of mankind. Commercially, a large number of drugs belonging to different classes, such as the Insulins, biguanides, sulfonylureas, meglitinides, and thiazolidinediones, DPP-4 inhibitors, SGLT2 INHIBITORS, and GLP1 AGONISTS are available to control and treat type 2 diabetic patients. However, none of these drugs are known to cure the diabetic phenotype completely. Furthermore, some of these agents can cause weight gain and have a limited role in the later stages of the disease. Newer formulations are reaching the market, which will help manage T2DM and improve patient outcomes.

The vast majority of cases of diabetes fall under two major categories of diabetes mellitus: Type 1 diabetes (T1DM), where the cause of hyperglycaemia arises as an absolute deficiency of insulin secretion. The occurrence of this

This type of diabetes among the population is identified by the evidence of an autoimmune pathologic process.

The second category of diabetes, named Type 2 diabetes (T2DM) is the most prevalent form that develops due to the combined action of both insulin resistance and insufficient insulin secretion.

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Here are some newer drugs that are available in India.

1.TIRZAPETIDE (Mounjaro)

- A new generation of dual GIP and GLP-1 agents
- Superior weight loss and HbA1c efficacy
- Once weekly dosing

Dual Mechanism:

(GLP-1) Glucagon-Like Peptide Receptor Agonist and (GIP) Glucose-Dependent Insulinotropic Polypeptide.[3]

Dosing

Initial: 2.5mg/ week x 4 weeks, then increase to 5mg/ week

The dose can be titrated by 2.5mg/ week every 4 weeks if further control is needed.

Maximum dose: 15mg/week

No renal dose adjustment/ cutoff

2. Liraglutide

- Brand Name: Victoza,
- Dosing: Once daily subcutaneous injection.
- Clinical Benefits: Proven efficacy in lowering HbA1c levels and promoting weight loss. It has cardiovascular benefits, reducing the risk of major adverse cardiovascular events in high-risk patients.

3. Semaglutide

- Brand Name: Wegovy (Ozempic), Rybelsus (oral formulation)

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- Dosing: Once weekly subcutaneous injection for Ozempic; once daily oral tablet for Rybelsus.

Clinical Benefits: Semaglutide has shown superior efficacy in glycemic control and weight loss compared to other GLP-1 receptor agonists. The oral formulation provides an alternative for patients who prefer non-injectable therapies.

4. Dulaglutide

- Brand Name: Trulicity
- Dosing: Once weekly subcutaneous injection.
- Clinical Benefits: Effective in reducing HbA1c and body weight. It also has cardiovascular benefits and is associated with a lower risk of hypoglycemia compared to traditional therapies.

Clinical Implications

Introducing newer GLP-1 receptor agonists in India has significant implications for diabetes management. Their ability to promote weight loss and improve cardiovascular outcomes makes them particularly useful in a population where obesity and heart disease are prevalent. The flexible dosing options, including once-weekly and oral formulations, enhance patient adherence and satisfaction.

Challenges and Considerations

Despite their benefits, GLP-1 receptor agonists are not without challenges. The cost of these medications can be a barrier to access for many patients in India, where healthcare affordability remains a concern. Additionally, potential side effects, such as gastrointestinal disturbances, must be communicated effectively to patients to ensure informed decision-making.

Conclusion

Newer GLP-1 receptor agonists represent a transformative advancement in managing Type 2 diabetes in India. Their multifactorial benefits extend beyond glycemic control to include weight management and cardiovascular protection. As healthcare providers become more familiar with these agents, they can optimize diabetes treatment strategies, ultimately improving patient outcomes. Ongoing education and awareness are essential to ensure that patients can benefit from these innovative therapies.[4]

5. Affreza – Inhaled Insulin

Affreza is an inhaled insulin formulation designed to provide an alternative to traditional insulin delivery methods for patients with diabetes. This research paper reviews the pharmacokinetics, efficacy, safety, and patient perspectives regarding Affreza, along with its potential role in diabetes management.

Affreza consists of insulin powder particles that are inhaled, allowing for rapid absorption into the bloodstream. Studies have shown that the pharmacokinetic profile of Affreza is distinct from that of subcutaneously injected insulin:

- Onset of Action: Affreza has a faster onset of action, typically within 12-15 minutes after inhalation, compared to 30 minutes for subcutaneous insulin.
- Peak Levels: The peak plasma insulin concentrations are reached within 30-60 minutes, allowing for better control of postprandial blood glucose levels.
- Duration of Action: The effects of Affreza last for approximately 2-3 hours, necessitating multiple doses throughout the day.

Efficacy

Clinical trials have demonstrated the efficacy of Affreza in managing blood glucose levels. In studies comparing Affreza to traditional rapid-acting insulin analogs, results indicate:

- Postprandial Glucose Control: Affreza significantly reduces postprandial glucose levels compared to placebo and shows comparable efficacy to injected insulin.
- Overall Glycemic Control: Patients using Affreza experienced similar reductions in HbA1c levels compared to those using subcutaneous insulin, with some studies indicating a preference for Affreza due to its ease of use.

Safety Profile

While Affreza offers benefits, its safety profile must also be considered:

- Respiratory Concerns: The primary safety concern associated with Affreza is its potential impact on lung function. Patients with asthma or chronic obstructive pulmonary disease (COPD) are cautioned against using inhaled insulin, as it may exacerbate respiratory issues.
- Hypoglycemia: Like all insulin therapies, Affreza carries a risk of hypoglycemia, particularly in patients who do not properly adjust their doses or dietary intake.

- Adverse Effects: Common side effects include cough, throat irritation, and a sensation of a dry mouth. These effects are generally mild and transient.

Patient Perspectives and Adherence

Patient adherence to diabetes treatment regimens is crucial for achieving optimal outcomes. The introduction of Affreza has been associated with increased patient satisfaction due to its non-invasive delivery method. Surveys and interviews with patients reveal:

- Ease of Use: Many patients prefer inhaled insulin over injections, reporting less anxiety and discomfort.
- Lifestyle Integration: Affreza's portability and ease of administration make it more compatible with active lifestyles, potentially improving adherence.

Future research should focus on long-term safety studies, potential applications in different patient populations, and ways to integrate Affreza into comprehensive diabetes management strategies.

Affreza inhaled insulin represents a significant advancement in diabetes treatment, offering a viable alternative to traditional insulin delivery methods. Its rapid onset of action and ease of use may improve patient adherence and satisfaction. However, careful consideration of safety concerns and patient education is essential for its effective implementation in clinical practice. Continued research and awareness will help maximize the benefits of this innovative therapy for individuals

6. Icodec – Once Weekly Insulin

Icodec is an analogue of human insulin, with three substitutions to the amino acid structure and an attached C20 icosane fatty diacid chain that allows the molecule to bind reversibly to albumin (similarly to insulin detemir), prolonging the half life to 196 hours (approximately 7 days) and achieving steady state after 3–4 once-weekly injections.[6] One unit of icodec provides the same glucose lowering as one unit of comparator daily basal insulins, with an equivalent once-weekly dose being seven times that of a daily basal insulin.[5]

In summary, insulin icodec offers similar or better glycaemic efficacy compared with daily basal insulin in type 2 diabetes, with good tolerability and encouraging safety results related to hypoglycaemia.[6] Although important clinical questions remain, reducing the number of basal insulin injections from 365 to 52 administrations per year may be a significant innovation in insulin management since its discovery more than a 100 years ago.

CONCLUSION

In conclusion, newer diabetic medications offer improved glycemic control and cardiovascular protection beyond traditional therapies, but require careful consideration of individual patient needs and potential side effects. Further research is crucial to optimize treatment strategies and address long-term outcomes, especially in the context of rising healthcare costs and disparities in access.

END NOTE

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