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A Systematic Review on Newer Drugs in Treatment of Type 2 Diabetes Mellitus

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Abstract:

As there is a rapid increase in patients with type 2 DM ,its treatment strategies were also being developed equally in the recent times. The pharmacological treatment varies in different individuals, Based on the comorbidities, treatment objectives and patient specific conditions.Along with hypoglycemics,weight management stratergies also plays a major role in controlling of glucose levels.

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are not only effective in decreasingglycemiabut also help withdecreasing the risk of comorbidities like cardiovascular and renal problems. Glucagon-like peptide-1 (GLP-1) receptor agonists promote weight loss and controls glucose levels. Novel glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 dual agonists, which stimulate both GIP and GLP-1 receptors, improveglycemic control and weight loss more compared to GLP-1 receptor agonists.Numerous innovative drugs are presently undergoing clinical development. [1]

Key words: Diabetes mellitus, Insulin, Glycemia, Glucose, Glycogenesis.

Introduction:

The American Diabetes Affiliation (ADA) and the European Affiliation for the Think about of Diabetes (EASD) agreement report in 2022 suggests more comprehensive and individualized administration for subjects with T2DM, taking into thought their particular circumstances and inclinations. Clinical trials of SGLT2 inhibitors (SGLT2i) and GLP-1 receptor agonists (GLP-1 RA) seems they will protect organs and improves in the management of cardio, renal complications, glycemic control. This increases the number of treatment options for T2DM.

Metformin was a first-line agent in the treatment of T2DM.Changes within the treatment of T2DM individually will improves the patient's quality of life.
Initially, administration of single glucose lowering agents accomplished glycemic control to lower the blood glucose levels, but these newer drugs will improve patient's quality of life by managing not only glycaemic conditions but also manages comorbid conditions of patients.
Diminished utilization of metformin as a first-line drug. Metformin could be a first-line treatment since it features a useful impact on HbA1C.Heart and renal problems are prompted to utilize a pharmaceutical such as a SGLT2i or GLP-1 RA, which is demonstrated to improvecardio-renal outcomes.[2]

Pathophysiology :

The blood glucose levels were maintained by certain harmones.

1.The stimulation of glucose from liver by glycogenolysis and gluconeogenesis, and also expanding of glucose by liver, muscle and fat tissue.

2. when the concentration of glucose is more then α cells of pancreas secretes Glucagon.
Action of Glucagon :It antagonizes glycogenolysis and gluconeogenesis in liver.

3.Along with glucogon,cortisol and catecholamines will improves the plasma glucose levels

4.Other hormones which are included in support of typical glucose level are:

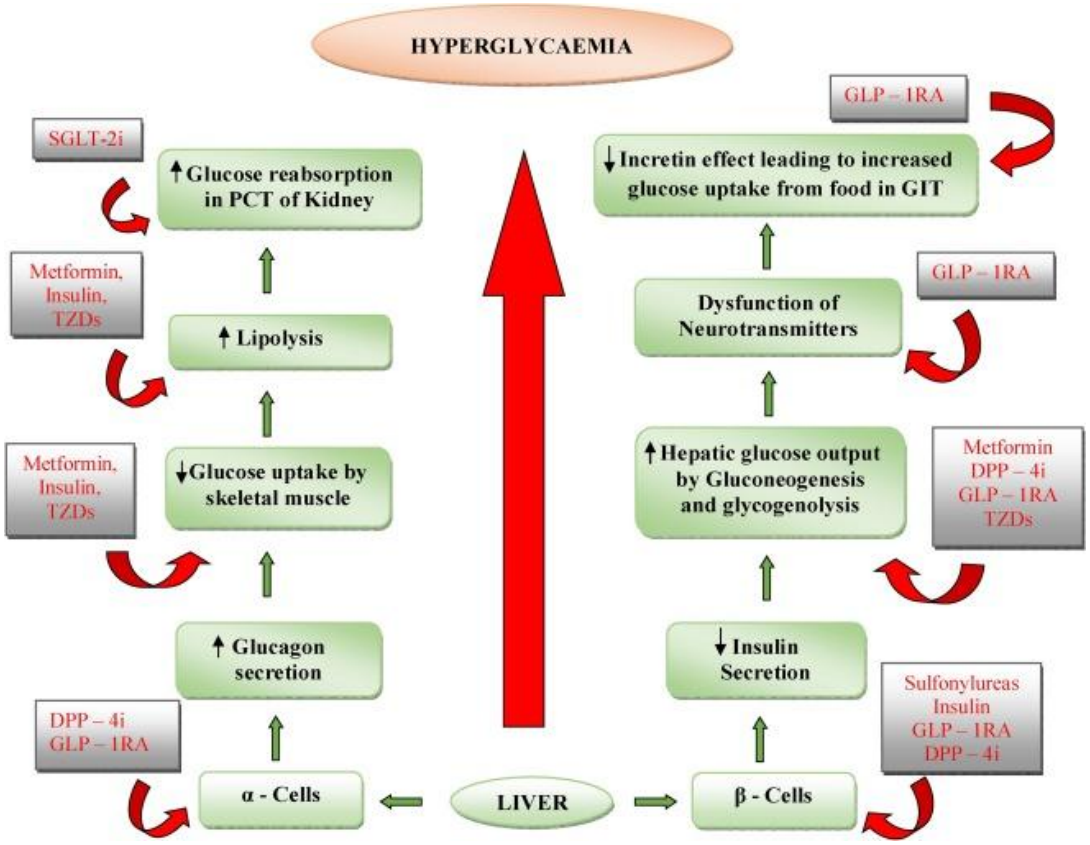
- Amylin (a 37 amino corrosive peptide),
- Glucagon like Peptide – 1 (GLP-1) (a 30 amino corrosive peptide) and
- Glucose subordinate insulinotropic polypeptide (GIP) (a 42 amino acid peptide) .

Glucose does not absorbed from digestive system, so transportation of glucose to the cells is doneby glucose transporters.

These transporters are of two types:

i)Sodium glucose co-transporter (SGLT)

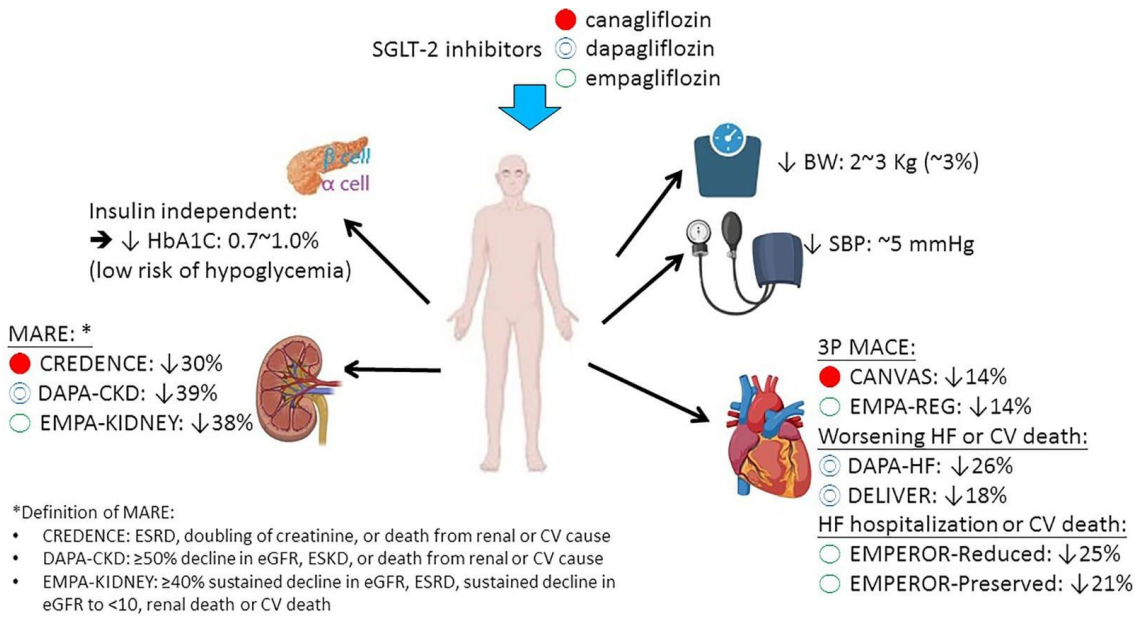
ii)Facilitative glucose transporter (Excess)



TREATMENT STRATERGIES DEVELOPED FOR GLYCEMIC CONTROL:

Inhibitors of SGLT2 (SGLT2i) :

SGLT2i for glucose regulation and its effects on the digestive tract In the S1 sections of the renal proximal tubules, SGLT2i binds SGLT2 proteins in a competitive manner. The prior inhibition of co-transporters leads to enhanced glucose/sodium excretion and decreased glucose and salt reabsorption. SGLT2i lowers the risk of hypoglycemia and has an impact that is not dependent on insulin.Dapagliflozin's seven components of action The proximal tubule of the nephron has an infinite number of sodium-glucose co-transporters. In dapagliflozin, these salt and glucose transporters are affected. Dapagliflozin has a broad effect on the SGLT-2 receptors in the order. This might be a transporter that simultaneously transports glucose and salt. The tubular film can be penetrated by both glucose and salt. However, a number of pump feathers that are visible on the basolateral subcaste can reabsorb them into the systemic rotation. The Na/K pump displays sodium for reabsorption into the frame, while GLUT-2 receptors display glucose for reabsorption. Dapagliflozin reduces the reabsorption of glucose by inhibiting the sodium glucose co-transporter-2. The excretion of glucose increases when the SGLT-2 is inhibited. Its exertional component, which is generated by the pancreatic β-cells, is not dependent on insulin. Dapagliflozin is a unique anti-diabetic drug since it can control blood sugar levels without the pancreas' assistance Colorful anti-diabetic drugs become less effective when β-cell function declines over time. Because dapagliflozin lozenges are acclimable and act without insulin (for example, insulin treatment causes cardiovascular issues), it also helps to better manage the additional adverse effects caused by other anti-diabetic treatments.Thus, dapagliflozin can be used in combination with other anti-diabetic drugs such pioglitazone, glimepiride, and metformin in a polytherapy setting to lower blood glucose levels.. SGLT2 medium filters and absorbs around 180g of glucose daily, whereas SGLT1 medium absorbs some of it as well. Because healthy individuals excrete almost no glucose, glucose levels are maintained in them to provide energy for diurnal conditioning. Because of this, it is linked to improved glycaemic management and reduced levels of glycated hemoglobin (Hb1Ac). [2]



GLP- 1 receptor agonist(GLP- 1 RA)

Mechanism of Action

In type 2 DM, GLP-1 Agonist acts on both alpha cells and beta cells. When there is an increase in the blood glucose levels, GLP-1 agonist acts on alpha cells, by blocking glucagon production. Along with this, it also likely decreases the apoptosis of pancreatic beta cells and promotes their proliferation. Pharmacologically, it is also capable of restoring insulin excretion.

Many studies have shown that this class of medications can reduce weight loss, and improve in cardiovascular outcomes along with glycemic control. GLP-1 agonists have their significant role in neuroprotection and decreased glucose production in liver. This class of drugs will decreases the mortality rate.[7]

Examples : Exenatide, Liraglutide, Dulaglutide, and Semaglutide

GLP-1 and GIP Dual Agonist (Tirzepatide)

This class of drugsis engineered by modifying the native GIP peptide sequence to enable binding to both GIP and GLP-1 receptors. Glucagon-like peptide-1 (GLP-1) receptor agonists already plays a potential role in treatment of type 2 diabetes (T2DM). Recent examples are the glucose-dependent insulinotropic polypeptides GLP-1 and GIP.

Tirzepatide, the most sophisticated unimolecular dual GIP/GLP-1 receptor agonist, is one example. Patients with type 2 diabetes receive this medication once a week via subcutaneous injection.

Depending on the risk-benefit ratio, dual or triple receptor agonists should be used to treat type 2 diabetes rather than unmodified GLP-1 receptor agonists.[8]

New Drugs Being Developed

Dual Receptor Agonists for Amylin/GLP-1:

In reaction to dietary intake, beta cells release insulin and amylin.. Amylin is a pancreatic islet cell hormone that suppresses postprandial glucagon secretion, thereby it also delays gastric emptying.

Example: Cagrilintide is a long-acting, weekly analog of amylin administered subcutaneously and is utilized both as monotherapy and in combination with the long-acting GLP-1 receptor agonist Semaglutide.

Conclusion:

Type 2 diabetes mellitus (T2DM) is becoming increasingly prevalent and represents one of the foremost significant risk factors for many complications. There has been recent improvements in the treatment of T2DM. Interventions vary concerning the method of treatment. Develpoments are ongoing, and these improvements in treatment may reduce complications and organs are protected, weight loss is achieved along with enhancing the quality of life for individuals living with T2DM.