IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Treatment Advances In Type 2 DM: A Comprehensive Review

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ABSTRACTS :-

Type 2 diabetes mellitus is a metabolic disease characterized by hyperglycemia and abnormal glucose level, fat, and protein metabolism [89,90]. The disease is due to insulin resistance in striated muscle tissue and a beta cell defect that inhibits the increase in insulin secretion to compensate for insulin resistance. Two classes of therapies, glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium-glucose cotransporter-2 inhibitors (SGLT-2i), have a lower risk of certain side effects, particularly hypoglycemia and weight gain, compared with many of the older medications for diabetes. Scientists develop a pancreas-mimicking system for responsive insulin delivery in diabetes treatment.

KEY WORDS :- DIABETES MELLITUS MEDICATIONS, INHIBITS ,SECRETION ,TREATMENT, DISEASE.

INTRODUCTION :-

Diabetes is a chronic disease characterised by hyperglycaemia, ultimately leading to microvascular (retinopathy, nephropathy, neuropathy) damage and to macrovascular (atherosclerotic ischaemic) events like myocardial infarction, cerebrovascular insults, and complications related to peripheral vascular disease, including the diabetic foot syndrome. The risk for neoplastic diseases is also increased in people with diabetes. Although the development of complications is higher in patients with associated obesity, arterial hypertension, lipid disorders, and a variety of other risk factors, it is also determined by glycaemic control (ie, the quantitative impact of exposure to high plasma glucose concentrations over a long period). Glucose-lowering therapy, therefore, remains a mainstay of diabetes management, in conjunction with a healthy lifestyle and with other medications specifically addressing the prevention or therapy of diabetes-related complications. The number of patients with diabetes and its proportion relative to the overall population is rising worldwide, and despite the development of numerous and quite successful novel treatment approaches (eg, continuous glucose monitoring, insulin pumps, sodium-glucose co-transporter-2 [SGLT2] inhibitors, glucagon-like peptide-1 [GLP-1] receptor agonists), the fraction of patients with well controlled diabetes has not risen as hoped for. This situation might in part be related to limited access (eg, high costs and lack of reimbursement by insurance policies), insufficient education of patients regarding the need for glycaemic control, and other reasons for so-called therapeutic inertia. However, it could hopefully be overcome by improving the glucoselowering efficacy of future diabetes medications, and by addressing mechanisms associated with fewer and less severe adverse drug effects

(weight gain, hypoglycaemia, and others). The search for new diabetes drugs undoubtedly is an active area of research and development.

OTHER FACTORS AFFECTING DISEASE PATHOGENESIS :-

Insulin resistance:

A primary factor in T2D, insulin resistance occurs when insulin-sensitive tissues don't respond properly to insulin. This can be caused by a number of factors, including inflammation, oxidative stress, and endoplasmic reticulum stress.

Defective insulin secretion:

Pancreatic beta cells may not secrete enough insulin.

Metabolic abnormalities:

T2D is associated with other metabolic abnormalities, such as dyslipidemia and hyperglycemia.

Environmental factors:

Environmental pollutants, such as bisphenol A, may alter beta-cell function.

Pathogens:

Certain pathogens, such as hepatitis C virus and herpes simplex virus type 1, may increase the risk of T2D.

Immune-mediated destruction:

Cytokines such as interferon gamma (IFN-γ), granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and transforming growth factor-β (TGF-β) may contribute to the destruction of beta cells. T2D is a chronic condition that causes persistently high blood sugar levels. It's a major component of metabolic syndrome (MS). While there's no cure for T2D, lifestyle changes and some medications can help prevent or put it into remission.

Advances in Management of Diabetes:-

The management strategy for the 29 million persons in the UnitedStates with either type 1 or 2 diabetes aims at achieving long-term glycemic control, which has been shown to be safe and to reduce the risk of microvascular disease over time (Table 2).42,47-50,52,56 Control of hyperglycemia has long-lasting effects that persist beyond the period of glycemic control, termed metabolic memory57 orlegacy effect. 48 In type 1 diabetes, intensivemetabolic control also reduces the risk of CVD45; however, the role of intensive glycemic therapy on CVD in type 2 diabetes remains less certain.58 Two clinical trials with long-term follow-up have shown a 15% to 17% reduction in CVD with intensive glycemic therapy,48,55 whereas others have shown no benefit52 or harm.51 Although this Review focuses on glycemic management, treatment of hypertension, and hyperlipidemia has a greater influence on mortality than control of glycemia among those with type 2 diabetes. For both type 1 and type 2 diabetes, smoking cessation and weight management are of major importance.Based on the Diabetes Control and Complications Trial (DCCT)42,56 and United Kingdom Prospective Diabetes Study (UKPDS)47,48 results and balancing long-term benefits and risks, the accepted metabolic goal for most people is anHbA1c level of less than 7%.18 Interventions to achieve this goal, commonly called intensive therapy, should be implemented as soon in the course of diabetes as possible. Patients who have projected lifespans that are too brief (eg, <5-10 years) to benefit from intensive therapy or who are at heightened risk from the hypoglycemic risks of the therapy, such as injury in patients engaged in potentially hazardous occupations, cases where risks outweigh benefits, should have their metabolic goals relaxed.18 The glucose levels necessary to achieve specific HbA1c levels have recently been determined based on empirical data.

Management of type 2 diabetes includes:

Healthy eating.

Regular exercise.

Weight loss.

Possibly, diabetes medication or insulin therapy.

Blood sugar monitoring.

These steps make it more likely that blood sugar will stay in a healthy range. And they may help to delay or prevent complications.

Some drugs used to treat type 2 diabetes include:

Incretin mimetics (GLP-1 receptor agonists): These injectable medications can help lower blood sugar levels and slow digestion. They can also help with weight loss and may reduce the risk of heart attack and stroke. Examples include:

Dulaglutide (Trulicity)

Exenatide (Byetta, Bydureon Bcise)

Liraglutide (Saxenda, Victoza)

Lixisenatide (Adlyxin)

Semaglutide (Ozempic, Rybelsus, Wegovy)

Sulfonylureas: These oral medications stimulate the pancreas to release more insulin. Examples include:

Glimepiride (Amaryl)

Glipizide (Glucotrol and Glucotrol XL)

Glyburide (Micronase, Glynase, and Diabeta)

Bile acid sequestrants (BASs): These oral medications can help lower blood glucose levels. The main BAS medication for type 2 diabetes is colesevelam (Welchol®).

Insulin: This is the oldest and most effective medication for lowering glycemia.

Other drugs: These include:

Voglibose

Alogliptin

Dapagliflozin

Saxagliptin

CONCLUSION:-

As mentioned in the Introduction section, since diabetes has a multifactorial pathological nature, it comes as no surprise that concurrent interactions of more than one potential modulator appear to have promise for future treatments. This may be achieved with a new approach, more specifically through the development of multi modal compounds. Unfortunately, the clinical development of some multifunctional ligands has been discontinued because of their undesirable side effects, maybe due to their imbalanced and/or supra-therapeutic activity. Given this, the potential promise of compounds able to modulate the activity of multiple targets still requires detailed investigations. Future advances in the understanding of the genetics base and of the signaling pathways which characterize the disease, coupled with their therapeutic applications, should lead to an expansion of new treatments, like personalized medicine [85,86], that could exploit new clinically available multi-target drugs. Tailoring medical therapies to the patient's biological characteristics may help to optimize disease treatment, thereby improving overall prognosis and decreasing comorbidities' risk.

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