

Recent trends in the therapeutic approach of type 2 diabetes mellitus

ABSTRACT –

Diabetes Mellitus is a metabolic condition that causes blood glucose levels to rise. (hyperglycemia). Type 2 diabetes mellitus, often known as NIDDM (non-insulin-dependent diabetes mellitus), is a disease in which cells do not adequately utilize insulin. Adult-onset diabetes is another name for it. It has become a significant health concern worldwide, but thanks to advancements in the medical sector and growing developments in treatment, diabetes may now be managed. The progress and treatment of diabetes mellitus help lower the health risks and complications associated with the disease. It is vital to undertake lifestyle modifications and therapy to ensure long-term diabetes control. Sulphonyl ureas, biguanides, and alpha-glucosidase inhibitors are among the latest medications to prevent blood glucose levels from rising too high. Patients who do not react to a single pharmacological therapy are given dual drug regimens. Nanotechnology, microtechnology, and statin therapy are some of the more recent treatments commonly employed to treat Diabetes Mellitus. This article examines the most recent trends or the advancements in therapeutic approaches for type 2 diabetes, focusing on progress over the last 10-15 years. This study aims to find out about the latest developments in the treatment of type 2 diabetes mellitus examine the merits and drawbacks of each option for DM management, and find a better cure for the disease. It will help decrease the mortality rate due to the growing rise of diabetes mellitus.

KEYWORDS- Type 2 DM, Treatment, antidiabetic, Insulin, Nanotechnology, advanced therapy

Introduction –

Diabetes mellitus has recently become a common metabolic condition. Diabetes has developed into a significant medical issue around life, affecting individuals of all ages, genders, cultures, and races, and its frequency has been increasing at an alarming rate. Over the next few years, the prevalence of type II Diabetes Mellitus is expected to skyrocket. By 2025, the number of people infected by Diabetes Mellitus is predicted to climb to 35 percent worldwide.^[1]

The word diabetes is derived from the original Greek word siphon, which means that individuals with diabetes "passed water." There are various varieties of diabetes, each with its cause. Types of diabetes are:

1. **TYPE 1 DIABETES MELLITUS-** This is caused to the loss of beta cells in the islets of Langerhans, which results in a shortage of insulin. Insulin-dependent diabetic Mellitus (IDDM) is another name for it. Degeneration of beta cells, viral infection, congenital abnormality of beta cells, and autoimmune disorders are all causes of type 1 diabetes mellitus.
2. **TYPE 2 DIABETES MELLITUS-** Insulin resistance, or the inability of insulin receptors to give an insulin response, is the cause. It is a type of diabetes mellitus that is more common. NIDDM stands for Non-insulin-dependent Diabetes Mellitus. Genetic abnormalities, stress, and lifestyle changes such as poor eating habits and physical inactivity are all factors that contribute to type 2 diabetes mellitus.

The three central relapses of insulin deficiency lead to various symptoms of diabetes.

1. Increased blood glucose levels due to decreased tissue utilization
2. Fat from adipose tissue is mobilized for energy reasons. As a result, the number of fatty acids in the body increases.
3. Recovery of protein from tissues

WAYS TO KEEP BLOOD GLUCOSE IN CHECK

- i. **Blood glucose testing:** Because structural components of blood cells are lacking, glucose concentrations in plasma or serum are 10-15% greater than in whole blood.
- ii. **Venous blood sample:** Enzymatic, colorimetric, and automated methods are routinely used in laboratories to determine plasma glucose levels.

iii. Capillary blood samples: Several strip-based portables battery-operated meters use the glucose oxidase method to test capillary blood samples. The latest gadgets use infrared absorption spectra to provide a non-invasive technique. ^[2]

Diabetes mellitus is a disease that can lead to various consequences, such as coronary heart disease, retinopathy, and neuropathy. It is now evident that maintaining tight blood glucose control lowers the risk of diabetes complications. Type II diabetes mellitus can be treated by oral hypoglycemic drugs.

The medications used to treat Type 2 Diabetes mellitus fall into three categories:

1. Insulin secretagogues are treatments that primarily stimulate insulin secretion.
2. Insulin sensitizers are drugs that make tissues (mainly the liver and adipose tissue) more sensitive to the action of insulin.
3. some medications primarily impact glucose absorption.

Oral drugs and insulin work in one of the following ways to treat diabetes:

1. Stimulates the pancreas to produce and secrete more insulin.
2. Slows the release of glucose from the liver (excess glucose accumulates in the liver).
3. Blocks carbohydrate digestion in the stomach or intestines, making tissues more insulin sensitive (and responsive).
4. Aids remove glucose from the body by increasing urination.

Recent developments in new drugs such as sulfonylureas, biguanides, and alpha-glucosidase inhibitors are used to lower blood sugar levels. Recent advances in drug-led discovery have led to the development of new classes of drugs, such as incretin mimetics, amylin analogs, GIP analogs, and dipeptide peptidase four inhibitors, that can potentially reduce diabetes.

Major drugs developed are (1) boosters of insulin release, (2) augmenters of insulin action, (3) inhibitors of glucose production in the liver, and (4) inhibitors of glucose uptake from the gut.

A compelling new drug has been developed that potentially reduces the risk of heart and kidney failure. Advances in technologies such as continuous blood glucose monitoring (CGM) systems and continuous subcutaneous insulin infusion are opening up new possibilities for improving blood glucose control. The number of new drugs available for

diabetes has exploded over the past decade, and notable new drugs are being developed to achieve this. Four thousand four hundred forty-four technological solutions target insulin delivery plus another hormone glucagon via 4,444 artificial pancreases, with system components already in use, with 4,444 suggesting that the above alternative may become available in the upcoming decade. This article aims to give a quick rundown of the most recent developments in diabetes treatment for therapeutic application. ^[3]

Objective- This review focuses on substantial advancements in the treatment of blood glucose in people with type 2 diabetes. The purpose of this paper is to offer a quick summary of recent DM management developments for clinical use.

Main text-

The recent therapies used in the treatment of Diabetes mellitus are

1. **Nanotechnology** New glucose estimation and insulin delivery methods have resulted from the application of nanotechnology to diabetes management.

Nanotechnology has been shown helpful in the treatment of diabetes mellitus by expanding the accessible surface area of the sensor-receptor complex and boosting the catalytic characteristics of electrodes. Improved oral formulations and islet encapsulation might transform insulin administration. Clinical nanotools are pore-encrusted microcapsules that might be used to administer medications. The holes present are so big t t it lets tiny atoms like oxygen, glucose, and insulin flow via, but small enough that larger and safer skeleton atoms 0proliferate. Diabetic patients can have microcapsules implanted beneath their skin with replacement islets of Langerhans cells, generally supplied from pigs. This might temporarily correct the body's defective glucose feedback loop without harsh immunosuppressive drugs, which could put the patient in danger of infection. Nanoparticle targeted drug delivery has the benefit of increasing medication bioavailability by targeting specific tissues, organs, and tumours and providing maximal doses of medicines directly to the target location.

Insulin is a critical component of type 1 and types 2 diabetes progression, and traditional insulin administration systems have been associated with infection, unpleasant dosing, and low patient compliance. On the other hand, recent micro and nanotechnology has made insulin administration easier by altering insulin delivery methods, such as pulmonary, nasal, transdermal, and closed-loop delivery. ^[3]

2. Gene therapy The most significant aspect of treatment is blood sugar control, which minimizes the number of problems connected with diabetes. For somatic cell gene therapy, there are two techniques of gene delivery that use the body's somatic cells. Ex vivo gene therapy is the initial procedure, defined as removing tissue from the body. Therapeutic genes are introduced in vitro and subsequently put back into the body, whereas in vivo treatment entails immediately providing a gene therapy vector to the patient via subcutaneous, intravenous, or bronchial channels or with the help of a local injection. Ex vivo therapy is used to produce cells that have beta-cell characteristics, such as insulin-producing cells. This technique has also been utilized to generate transplantable cells.

Transgenes like glucokinase, for example, impact the liver by reducing glucose levels. The insulin gene can be altered to produce single-chain insulin with 20-40 times the activity of mature insulin. The delivery of genes that signify a glucose response and gene therapy to boost β -cell formation in the liver are two more fields of genetic engineering. The stimulation of cell production in the liver was also investigated. Endocrine cells can be induced to create β -cells by delivering islet-specific transcription factors, according to Kojima et al. ^[3]

3. Statin therapy Statins are blockers of 3-hydroxy-3-methylglutaryl coenzyme A, which block a crucial process of LDL cholesterol in the liver, decreasing blood cholesterol levels and improving blood vessels lining health. Statins (HMG Co-A reductase inhibitors) are crucial medications for persons with type 2 diabetes who want to diminish their risk of heart disease. Statins are significantly efficient in lowering cardiovascular disease in those with moderate serum cholesterol and no prior history of cardiovascular disease. On the other hand, HMG-CoA reductase inhibitors or statin therapy may cause side effects such as renal failure. Young and disease-free persons were found to be inefficient or poorly adherent to statin prescription in a trial of 6422 patients, according to Journal of Diabetes research. However, treatment should focus on older patients considering younger patients are less compliant. Patients with high-risk factors and evidence of heart disease should also be given statins. ^[4,5]

4. Medical Nutrition Therapy Numerous improvements in clinical research aimed at using the diet to treat illnesses and diseases have led to nutritional therapy in preventing and treating diabetes. Sustaining optimal blood lipid levels, appropriate body weight, and normoglycemic levels are the goals of a diabetic diet. Nutritional therapy as a diabetes

treatment will be determined by the patient's age-related nutritional requirements and specific factors such as food preferences, other medical conditions, exercise regimen, and recommended nutritional requirements based on the patient's ability and health status. ^[5]

5. Stem cell technology Researchers may use stem cell research to generate specific types of human cells in the lab and study how they behave and interact under various settings. DM can be prevented by either eliminating abnormalities in pancreatic beta cells or enhancing the sensitivity of the body's cells to insulin action. While B-cell replacement procedures provide unique sources, existing islet and pancreatic transplantation strategies are constrained by a scarcity of donor organs. Because of its immunosuppressive qualities, soluble Mesenchymal stem cell (MSC) therapy has become a preferred treatment for type 1 DM. Because of the direct contact and generation of markers, MSCs have been reported to exert immunomodulatory effects in vitro and in vivo. For type 1 DM patients with poor glycemic control, clinical pancreatic or islet transplantation has been regarded as a viable therapy option. Researchers gathered and evaluated 13 papers published between 2006 and 2016 that included 342 patients who got stem cells similar to those found in cord blood and another 111 who received stem cells similar to those found in cord tissue to treat their diabetes.

6. Herbal therapy For a lengthy moment, researchers have advocated for using tiny dosages of insulin and non-insulin-dependent diabetic Mellitus in locally generated prescriptions to treat diabetes. Plants with anti-diabetic qualities could be used to supplement current medications or as a proposed source for new hypoglycemic mixes. Researchers have long advocated for the use of small insulin and non-insulin secondary diabetes to treat locally created diabetes mellitus using local prescriptions. Plants with anti-diabetic qualities could be used to supplement current medications or as a proposed source for new hypoglycemic mixes. For insulin-dependent and non-insulin-dependent diabetic Mellitus, researchers have long proposed running-home recipes. Plants with anti-diabetic qualities could be used to supplement current medications or as a proposed source for new hypoglycemic mixes. Herbal medicines are trendy among the general public due to their low cost and lack of controversy. The stimulation of cell production in the liver was also investigated. Endocrine cells can be induced to create β -cells by delivering islet-specific transcription factors, according to Kojima et al. ^[6]

7. Leptin Therapy Leptin is a hormone produced by fat cells that affects central nervous system neurons. It prevents overheating by reducing food intake and raising energy expenditure. By activating leptin receptors, it lowers blood sugar levels.

RECENT DRUGS-

Sulfonylureas (SU) of the first generation were launched to successfully replace oral insulin in most patients with type 2 diabetes at the time. Ten-year research by a university group (comparing tolbutamide to insulin or a single diet) found that glucocorticosteroids may increase cardiovascular disease mortality, but the findings were extensively contested and subsequently dismissed. The second generation of sulfonylureas is still widely used. Since the emergence of thiazolidinediones as the primary oral insulin sensitizer around the turn of the century, insulin occlusion has steadily dominated a "pancreatic-centric" strategy focusing on type 2 diabetes mellitus. The central MOA concept is to "eat up" free to avoid lipotoxicity. They are the peroxisomal proliferation receptor (PPAR) gamma receptors agonists, mainly found in adipose tissue. ^[7]

COUNTER REGULATORY HORMONES

By promoting liver glycogenolysis and gluconeogenesis, these compounds raise blood sugar levels. From a therapeutic aspect, specialists who interfere with the release or countermeasures of controlled substances can be advantageous. Glucocorticoids' worst enemy: Body bloating, insulin blockage, and hyperglycemia can all be caused by an increase in glucocorticoid concentrations, and any treatment that reduces glucocorticoid activity will lessen these antagonistic effects. ^[8] In giant diabetic rodents, specific inhibitors of 11 HSD1 have been demonstrated to increase insulin-dependent capacity, glycemic control, and subsequent development of plasma lipids. Insulin is necessary for persons with type 2 diabetes who have had poor results with sulfonylureas.

SGLT2 (sodium-glucose transporter 2) inhibitors block glucose and sodium reabsorption in the proximal tubule, are the last class of drugs proposed for diabetes. Up to 60 g of glucose is excreted per day, resulting in a drop in blood sugar without insulin and calorie loss, resulting in weight loss. The inhibition of SGLT2 is insufficient and is somewhat compensated by the prolongation of SGLT1 tubular movement. Even though the number of SGLT2 and SGLT1 inhibitors is growing,

equilibrium remains a problem. Endogenous gluconeogenesis is also increased, most likely due to glucagon stimulation, which can be avoided by connecting glucagon to scrutinized TLDs. SGLT2 inhibitors similarly reduce cyclic stress, but the composition is unknown. Inhibitors of 11 β -selective hydroxysteroid dehydrogenase type 1 (11BHSD1) 11BHSD1 inhibitors show a lot of promise for treating osteoporosis and metabolic syndrome, which includes type 2 diabetes. Anti-diabetic, anti-adipogenic, and anti-lipogenic characteristics of BHSD1 inhibitors, as well as anti-osteoporotic activity. ^[9]

Mimic Amylin, a glucose regulator produced by islet beta cells, is released alongside insulin and deposited in the islets of diabetes patients. It appears to play a role in promoting satiety, slowing stomach emptying, and suppressing glucagon secretion. It also activates G protein-coupled receptors and activates a variety of common intracellular signal transduction pathways, ultimately leading to cell death. ^[10-16]

Conclusion

In most countries, preventing type 2 diabetes mellitus is a top priority to stem the expanding epidemic. In the twenty-first century, the treatment of type 2 diabetes mellitus has progressed toward safer and maybe more effective medications, which in some situations can also minimize the risk of cardiovascular and renal complications. Over the past two decades, research on the pathophysiology of DM has progressed at an alarming rate. A better knowledge of diabetes has aided the development of medication classes that target specific metabolic pathways. Significant advances in blood sugar management in type 2 diabetes have led to the control of diabetes and potentially reduced mortality. Over the past decade, the incidence of kidney and heart-related diseases in people with DM has decreased significantly. Treating the DM disorder is multifactorial. The development of PCR, DNA microarrays, and qualitative knockout via sedation has opened up another realm of striking validation of imperfect traits/changes in the genome of living things. Diet, exercise, and diabetes education are still essential components of diabetes management. Obesity should be approached aggressively, and emphasize lifestyle changes. There is hope for a better future for diabetes as a variety of new and effective technologies for the treatment of diabetes emerge.

NOTE:

The study highlights the efficacy of "Herbal medicines, " an ancient tradition used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors

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