IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

OVERVIEW ON THERAPEUTICAL MANAGEMENT OF DIABETES – MONOTHERAPY, COMBINATIONAL THERAPY

Jhansi rani. kokkiligadda[1], *Rahul. Ariga*[2],*Dr. D. Ashok kumar reddy*[3]

Authors1,2- doctor of pharmacy, correspondent author 3- Dr.D.Ashok Kumar reddy, Department of pharmacology.

PHARM.D Students, Department of pharmacology, A.M Reddy Memorial College of Pharmacy, Petlurivaripalem, Narsaraopeta

ABSTRACT:

Diabetes is a chronic disease that has an impact on how your body uses food as fuel. It is broadly divided into two main categories diabetes mellitus and diabetes insipidus. Diabetes mellitus is divided into type 1, type 2and gestational diabetes. The main causes of diabetes include diet, physical inactivity, obesity, family history. Glycosylate HbA1c express glucose or glycemic control for 2-3 months, the recommended level of normal HbA1c is below 7%.Type 1 diabetes is an insulin dependent where as type 2 is an co-existence of insulin deficiency and insulin resistance. Gestational diabetes occurs in some pregnant women and goes away after pregnancy. Therapy for type 1 diabetes include synthetic insulin supply where as for type 2 diabetes oral anti diabetic agents are used as an first line therapy. There are seven classes oral of anti diabetic drugs 1.biguanides,2.Sulfonyluras,3.Meglitinides,4.DPP-4 inhibitors,5.thiazolidinediones,6.SGLT2 -inhibitors,7.alpha glucosidase inhibitors. The second line therapy includes combination of two oral hypoglycemics or a combination of oral antidiabetic drug and insulin. The combinational therapy was used when the monotherapy fails to provide the glycemic control.

Keywords: Diabetes, hypoglycemics, insulin resistance, biguanides, meglitinides, sulfonylureas, SGLT2 inhibitors, alpha glucosidase inhibitors,DPP4 inhibitors ,glycemic control

INTRODUCTION:

Diabetes develops when body cells are unable to absorb sugar[glucose] and use it as fuel. As a result additional glucose begins to accumulate in the bloodstream. Uncontrolled diabetes can have dangerous side effects, including damage to many body organs and tissues such as heart, kidneys, eyes, nerves. The reason behind high glucose levels is body breaks down the food you eat into different nutrient sources as apart of digestion process. It converts carbohydrates to glucose. When glucose is in bloodstream it needs assistance -a -key- to enter into body cells, which make up your body tissues and organs and are where it will be utilised. Insulin serves as this key. The gland that makes hormone insulin is located behind the stomach in the pancreas. In the case of diabetes pancreas either does not produce any insulin or not enough of it or your body cells can't utilise the insulin properly that is produced as they do not respond to it. Diabetes is divided into two types diabetes

mellitus and insipidus. In diabetes mellitus blood glucose is too high and kidneys try to remove the extra glucose by passing it in urine. As in case of diabetes insipidus glucose levels are normal, but your kidney can't properly concentrate urine. Diabetes mellitus is divided into four types. They are type 1 diabetes, type 2 diabetes, prediabetes, gestational diabetes.

Type 1 DIABETES: It is an autoimmune disease meaning your body attacks itself. In this case the insulin producing cells in pancreas i:e beta cells are destroyed.it is usually diagnosed in children and adults. Juvenile diabetes used to be a more common name for it. It is an insulin dependent diabetes.

TYPE 2 DIABETES: Type 2 diabetes is a chronic disease characterized by coexisting insulin deficiency and insulin resistance, with consequent hyperglycemia leading to micro- and macrovascular complications. Type 2 diabetes is most typical form of diabetes.

PREDIABETES: This type is the pre-stage of type 2 diabetes. Your blood sugar is higher than normal, but not high enough to formally diagnose type 2 diabetes.

GESTATIONAL DIABETES: It develops in some women during pregnancy and usually disappears after pregnancy. However, if you have gestational diabetes, you are at an increased risk of developing type 2 diabetes.

THERAPY:

TYPE 1 DIABETES:

People with type 1 diabetes require synthetic insulin several times each day to live a healthy life. The three main components of type 1 diabetes management include insulin, blood sugar monitoring, and carbohydrate counting.

TYPE 2 DIABETES:

Type 2 diabetes influences about two hundred million human beings worldwide, together with extra than 1 / 4 of the aged in evolved countries. Diet and exercise, together with oral antidiabetic drugs, are first-line treatments to gain the aim of enhancing glycemic control. When glycemic control is not established or if HbA1C increases to 6.5% after 2-3 months of lifestyle modification, pharmacological treatment for T2DM should be started. There are eight pathophysiological pathways underlying in type 2 diabetes.These include - Reduced insulin secretion from pancreatic beta-cells, increased glucagon secretion from pancreatic alpha-cells, increased glucose production in the liver, increased lipolysis, increased renal glucose reabsorption, decreased incretin effect in the small intestine, and impaired or diminished glucose uptake in peripheral tissues like skeletal muscle, liver, and adipose tissue are just a few of the effects. Neurotransmitter dysfunction and insulin resistance are also among them. Currently accessible treatments to reduce blood sugar focus on one or more of these important routes. Biguanides, sulfonylureas, meglitinide, thiazolidinedione (TZD), dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter (SGLT2) inhibitors, and -glucosidase inhibitors are the main groups of oral antidiabetic drugs.

Combination therapy with two oral medicines or with insulin may be recommended if the HbA1C level climbs to 7.5% while you're taking your medication or if your baseline HbA1C is below 9%.

Despite the fact that these drugs can be administered to all patients regardless of their weight, some drugs, such as liraglutide, may be particularly beneficial for obese diabetics as opposed to lean diabetics

BIGUANIDES:

The primary first-line oral medication of preference for the treatment of T2DM across all age categories is the biguanide metformin. Through intricate interactions with the mitochondrial enzymes, metformin activates the liver's adenosine monophosphate-activated protein kinase, causing hepatic absorption of glucose and blocking gluconeogenesis.

Additionally, it increases tyrosine kinase activity and insulin sensitivity by promoting insulin receptor expression. The prevention of CVDs may also be achieved by metformin by lowering plasma lipid levels via a PPAR- route, according to recent research. The incretin-like effects of glucagon-like peptide-1 (GLP-1) may

be responsible for the reduction in food intake. Thus, modest weight loss may be induced by metformin in diabetics who are overweight or obese.

GLP-L RECEPTOR AGONISTS:

Exenatide and liraglutide are the two GLP-1 receptor agonists that are currently on the market. These medicines have a higher resistance to DPP4's enzymatic destruction. Consider treating young individuals with GLP-1 analogues, which would help with weight loss and ameliorate metabolic dysfunction, if they have recently been diagnosed with T2DM, central obesity, and an aberrant metabolic profile. GLP-1 analogues should not be used in cases of renal failure.

DPP4-INHIBITORS: Sitagliptin, saxagliptin, vidagliptin, linagliptin, and alogliptin are dipeptidyl peptidase 4 inhibitors. These drugs can be taken alone or in combination with TZD, metformin, or sulfonylurea. This medication is comparable to other oral diabetes medications. There is no evidence that gliptins increase the frequency of hypoglycemia incidents as compared to controls. Inhibitors of dipeptidyl peptidase 4 affect postprandial lipid levels. In T2DM patients who have never taken these drugs before, vidagliptin treatment for four weeks reduces postprandial plasma triglyceride and apolipoprotein B-48-containing triglyceride-rich lipoprotein particle metabolism following a fatty meal. It has been proven that sitagliptin therapy improves coronary artery perfusion and cardiac function in diabetic patients with coronary heart disease.

SGLT2 INHIBITORS:

Canagliflozin, dapagliflozin, and empagliflozin are new kinds of glucosuric medications called sodium-glucose cotransporter inhibitors.By preventing glucose reabsorption in the proximal renal tubule by inhibiting SGLT2, SGLT2 inhibitors lower blood sugar without the use of insulin (38). Due to their glucose-independent mechanisms of action, these medications may be useful in T2DM that has progressed to the point where pancreatic beta-cell reserves have been irreparably depleted. These medications help reduce blood pressure and modestly reduce body weight. SGLT2 inhibitors may cause vaginal mycosis, urosepsis, and pyelonephritis in addition to urinary tract infections. Rarely, SGLT2 inhibitors can lead to ketoacidosis. If a patient has symptoms of ketoacidosis (including frank nausea or vomiting, or even non-specific signs like fatigue or abdominal pain), they should stop taking their SGLT2 inhibitor and get medical help right once.

SULFONYLUREAS:

Sulfonylureas increase insulin release in the pancreas by inhibiting KATP channels, which lowers blood glucose levels. They restrict liver gluconeogenesis as well. Sulfonylureas lessen the liver's ability to clear insulin and impede the breakdown of lipids to fatty acids . Sulfonylureas are currently recommended as supplemental or second-line treatments for T2DM.First-generation agents, which include chlorpropamide, tolazamide, and tolbutamide, and second-generation medicines, which include glipizide, glimepiride, and glyburide, are separated into two classes. In comparison to second-generation sulfonylureas, first-generation sulfonylureas are known to have longer half-lives, a higher risk of hypoglycemia, and a later beginning of action.

MEGLITINIDES:

Meglitinides, which include repaglinide and nateglinide, are non-sulfonylurea secretagogues that were authorised for use as a T2DM therapy in 1997. Meglitinide interacts to the sulfonylurea receptor in the pancreatic -cells via a similar manner to sulfonylureas. Meglitinide is a short-acting insulin secretagogues because its affinity to the receptor is lower than that of sulfonylurea, which allows for more flexibility in how it is administered. It is also less efficient than sulfonylurea because a greater blood sugar level is required before it can activate -cells to secrete insulin. If a patient experiences late postprandial hypoglycemia while taking a sulfonylurea or has an inconsistent eating pattern, rapid-acting secretagogues (meglitinides) may be used in place of sulfonylureas.

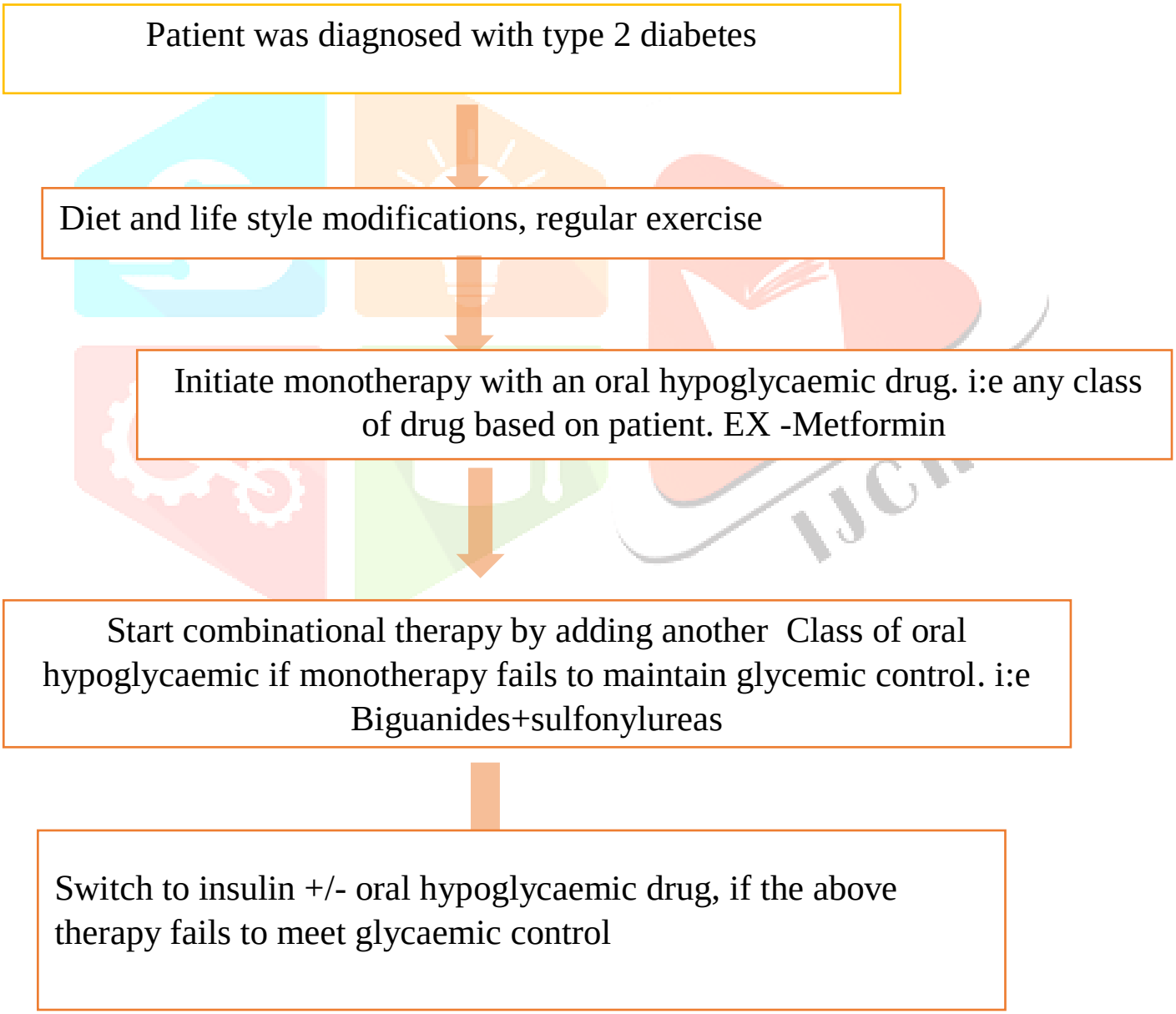
THIAZOLIDINEDIONE:

TZDs enhance insulin activity similarly to biguanides. Pioglitazone and rosiglitazone serve as representatives. TZDs are PPAR agonists that promote greater glucose absorption in a variety of tissues, including adipose, muscle, and liver. The mechanisms of action include decreased accumulation of free fatty acids, decreased levels of inflammatory cytokines, increased levels of adiponectin, and preservation of -cell integrity and function, all of which reduce insulin resistance and -cell exhaustion. The hazards outweighing the benefits, though, is a major worry. Heart failure is brought on by combined insulin-TZD treatment. TZDs are therefore not favoured as first-line or even step-up therapy.

COMBINATIONAL THERAPY

The most effective treatment for lowering elevated glucose levels is insulin therapy. Insulin should be administered to individuals who are unable to control their blood sugar levels with a combination of oral hypoglycemic medications. The first step is mixing insulin with the oral hypoglycemic medications that have already been administered.

MANAGEMENT OF TYPE 2 DIABETES:



Management of diabetes based on HbA1C levels

<table>
<tr><td rowspan="2">PARAMETERS</td><td rowspan="2">HIGHER LEVELS PREFERENCES</td><td colspan="3">MANAGEMENT OF DIABETES</td></tr>
<tr><td>FIRST LINE THERAPY</td><td>Second line therapy</td><td>Combination therapy</td></tr>
<tr><td rowspan="4">HbA1C</td><td><9%</td><td>Monotherapy with Metformin</td><td>Continue and monitor metformin</td><td colspan="2">-</td></tr>
<tr><td>>9%

Asyptomatic</td><td rowspan="3">-</td><td rowspan="3">-</td><td colspan="2">Consider Dual OHA agents</td></tr>
<tr><td>FIRST CHOICE</td><td>SECOND CHOICE</td></tr>
<tr><td>1.SU

2.DPP-4 inhibitors

3.SGLT2 inhibitors</td><td>1.AGI

2.Glinides

3.TZD

4.GLP 1RA</td></tr>
<tr><td>Symptomatic</td><td>Consider insulin</td><td>-</td><td colspan="2">-</td></tr>
</table>

CONCLUSION:

Diabetes is a chronic metabolic disease, divided into four types called type 1diabetes, type 2 diabetes, prediabetes and gestational diabetes. The normal range of HbA1C is 7%. Diabetes can be managed by oral hypoglycaemics as monotherapy when the HbA1C rises to above 7% while diet control and life style modifications fails to give glycaemic control. And if the HbA1C climbs up to 7.5 and above while the patient is on oral hypoglycemics combinational therapy with insulin as second line therapy is used.

REFERENCES

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4034109/
- https://my.clevelandclinic.org/health/articles/12070-oral-diabetes-medications
- https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006992.pub2/epdf/abstract
- https://my.clevelandclinic.org/health/diseases/7104-diabetes-mellitus-an-overview
- https://www.diabetes.org.uk/diabetes-the-basics/types-of-diabetes
- https://pubmed.ncbi.nlm.nih.gov/16702795/
- https://pubmed.ncbi.nlm.nih.gov/19555131/
- https://www.cochrane.org/CD006992/ENDOC_combinations-insulin-and-oral-glucose-lowering-drugs-people-type-2-diabetes-insulin-treatment
- https://pubmed.ncbi.nlm.nih.gov/12365467/
- https://main.icmr.nic.in/sites/default/files/guidelines/ICMR_GuidelinesType2diabetes2018_0.pdf
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4366766/
- https://www.thelancet.com/journals/landia/article/PIIS2213-8587(19)30069-5/fulltext
- https://www.amjmed.com/article/s0002-9343(13)00487-7/fulltext
- https://diabetesjournals.org/care/article/39/Supplement_2/S137/30104/Clinical-Considerations-for-Use-of-Initial
- https://www.cochrane.org/CD012368/ENDOC_metformin-and-sulphonylurea-combination-therapy-adults-type-2-diabetes-mellitus