Common oral diabetes drugs involved in treatment of diabetes.

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Introduction

Diabetes Mellitus (DM) is a chronic disorder characterised by a high blood glucose level (hyperglycemia), which is caused by defects in insulin secretion, action, or both. Patients are at significant risk for long-term macro- and microvascular problems as a result of the chronic metabolic imbalance associated with this disease, which can lead to recurrent hospitalisation and consequences, including an increased risk of Cardiovascular disease if not treated properly (CVDs).

Biguanides, sulfonylureas, meglitinide, Thiazolidinedione (TZD), dipeptidyl peptidase 4 (DPP-4) inhibitors, Sodium-Glucose Cotransporter (SGLT2) inhibitors, and alpha-glucosidase inhibitors are the most common oral diabetes drugs. Combination therapy with two oral medications, or insulin, may be considered if the HbA1C level climbs to 7.5 percent while on medication, or if the baseline HbA1C level is 9% [1].

Biguanide

Biguanide and its derivatives were first discovered in the Middle Ages for the treatment of diabetes. The herbaceous plant Galega officinalis was discovered to contain guanidine, galegine, and biguanide, all of which lower blood glucose levels. Metformin is a biguanide that is the most commonly prescribed oral treatment for T2DM in people of all ages. Metformin inhibits gluconeogenesis by activating adenosine monophosphate-activated protein kinase in the liver, inducing hepatic glucose absorption and reducing gluconeogenesis via complicated actions on mitochondrial enzymes [2].

Metformin is well tolerated, with few side effects, a low risk of hypoglycemia, and a low likelihood of weight gain. Metformin has been found to slow the progression of T2DM, lower the risk of complications, and lower death rates in patients by reducing hepatic glucose synthesis (gluconeogenesis) and increasing insulin sensitivity in peripheral tissues. It also enhances insulin sensitivity by increasing tyrosine kinase activity and activating insulin receptors. Metformin may help reduce CVDs by lowering plasma lipid levels via a peroxisome proliferator-activated receptor (PPAR)-dependent mechanism. Incretin-like activities mediated by glucagon-like peptide-1 (GLP-1) could reduce food intake. Metformin may therefore cause modest weight loss in diabetics who are overweight or obese [3].

Incretin mimetics

The differential in insulin secretory response from an oral glucose load versus glucose delivered intravenously is known as the incretin effect. After oral glucose ingestion, the incretin effect is responsible for 50–70% of total insulin production. The two naturally occurring incretin hormones that play key roles in glycemic control are glucose-dependent insulinotropic polypeptide (GIP, or incretin) and glucagon-like peptide (GLP-1); these peptides have a short half-life since DPP-4 inhibitors hydrolyze them within 90 minutes.

The incretin effect is diminished or nonexistent in persons with T2DM. GIP's insulinotropic effect is diminished in T2DM patients in particular. Incretins cause weight loss by slowing down gastric emptying. Because of their weight-loss effects, these drugs may become more popular among diabetics [4].

SGLT2 inhibitors

New glucosuric drugs called sodium-glucose cotransporter inhibitors include canagliflozin, dapagliflozin, and empagliflozin. SGLT2 inhibitors impede glucose reabsorption in the proximal renal tubule, resulting in insulin-independent glucose reduction.

These medications may be useful in advanced stages of T2DM when pancreatic beta-cell reserves have been permanently depleted due to their glucose-independent mechanism of action. These medications help you lose weight and lower your blood pressure. SGLT2 inhibitors can cause urinary tract infections such urosepsis and pyelonephritis, as well as genital mycosis. Ketoacidosis is a rare side effect of SGLT2 inhibitors. If patients experience signs of ketoacidosis, they should stop taking their SGLT2 inhibitor and seek medical help right away.

Insulin

If non-insulin monotherapy with metformin at the maximum tolerable dose fails to achieve or maintain the A1C target after three months, a second oral drug, a GLP-1 receptor agonist, or basal insulin may be added to the regimen. Insulin therapy (with or without additional agents) should be started in patients with newly diagnosed T2DM who are symptomatic (catabolic features such as weight loss, ketosis, or hyperglycemia features such as polyuria/polydipsia) and/or have severely elevated blood glucose levels [300–350 mg/dL (16.7–19.4

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mmol/L) or A1C [≥ 10–12%] and/or severely elevated blood glucose levels [5].

Thiazolidinedione

TZDs, like biguanides, enhance insulin sensitivity. Representative agents are rosiglitazone and pioglitazone. TZDs are PPAR agonists that promote glucose absorption in a variety of tissues, including adipose, muscle, and liver. Free fatty acid accumulation is reduced, inflammatory cytokines are reduced, adiponectin levels rise, and Beta-cell integrity and function are preserved, all of which lead to improved insulin resistance and Beta-cell exhaustion.

Other glucose-lowering pharmacologic agents

Pramlintide is an amylin analogue that slows stomach emptying, reduces glucagon release from the pancreas, and increases satiety. It's an FDA-approved T1DM treatment for adults. Pramlintide causes weight loss while also lowering insulin levels. To avoid severe hypoglycemia, prandial insulin dose must be reduced at the same time. Bromocriptine, alpha-glucosidase inhibitors like voglibose and acarbose, and bile acid sequestrants like colesevelam are some other medications that can help lower blood sugar. Metformin sequesters bile acids in the intestinal lumen, decreasing lipid levels; however, the same process may also lead to gas generation and gastrointestinal problems.

Conclusion

Renal failure, ASCVD, non-traumatic lower limb amputation, blindness, and mortality are all common complications of type 2 diabetes. It's a serious chronic medical illness that necessitates the collaboration of a multidisciplinary team of healthcare providers, dietitians, patient educators, patients, and their families. All patients with diabetes require lifestyle interventions to manage their weight and treat obesity, as well as patient education. Treatment choices and medication(s) may be tailored to a patient's risk factors, current HbA1C level, pharmaceutical efficacy, simplicity of use, financial situation/insurance/costs, and risk of negative side effects such hypoglycemia and weight gain. The effectiveness of medication should be assessed as frequently as possible using diagnostic blood tests (HbA1C) and monitoring for diabetes complications.

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