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Genetic Contribution and Inhibitor Marker of Diabetic Disease: A Review Article

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ABSTRACT

Introduction: Currently available glucose-lowering therapies target one or more of the treatment pathways. The patient approach should be used for multiple pharmacological options. Factors to consider include efficacy, cost, potential side effects, weight gain, comorbidities, risk of hypoglycemia, and patient preference. Pharmacological treatment should be initiated when glycemic control is not achieved or if HbA1C increases to 6.5% after 2-3 months of lifestyle intervention.

Discussion: Therapy with oral medication should be started in conjunction with intensive lifestyle management. The major classes of oral antidiabetic drugs include biguanides, sulfonylureas, meglitinides, thiazolidinedione (TZD) inhibitors, dipeptidyl peptidase 4 (DPP-4), sodium-glucose cotransporter (SGLT2) inhibitors, and -glucosidase inhibitors. If the HbA1C level increases to 7.5% during treatment or if the baseline HbA1C is 9%, combination therapy with two oral agents, or with insulin, may be an option. Although this drug can be used in all patients regardless of their weight, some drugs such as liraglutide may have distinct advantages in obese patients compared to lean diabetics.

Conclusion: Inhibitors is for patients not receiving an intensive insulin regimen. According to current guidelines, HbA1C levels should be assessed regularly in all diabetic patients. The frequency of HbA1C testing is flexible and depends primarily on the patient's response to therapy and the physician's judgment. HbA1C testing is performed at least every 6 months for patients who are meeting treatment goals.

KEYWORDS: Diabetic disease; Inhibitor; Lifestyle; Marker; Treatment

INTRODUCTION

Currently available glucose-lowering therapies target one or more of the treatment pathways. The patient approach should be used for multiple pharmacological options. Factors to consider include efficacy, cost, potential side effects, weight gain, comorbidities, risk of hypoglycemia, and patient preference. Pharmacological treatment should be initiated when glycemic control is not achieved or if HbA1C increases to 6.5% after 2-3 months of lifestyle intervention [1].

Therapy with oral medication should be started in conjunction with intensive lifestyle management. The major classes of oral antidiabetic drugs include biguanides, sulfonylureas, meglitinides, thiazolidinedione (TZD) inhibitors, dipeptidyl peptidase 4 (DPP-4), sodium-glucose cotransporter (SGLT2) inhibitors, and -glucosidase inhibitors. If the HbA1C level increases to 7.5% during treatment or if the baseline HbA1C is 9%, combination therapy with two oral agents, or with insulin, may be an option. Although this drug can be used in all patients regardless of their weight, some drugs

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such as liraglutide may have distinct advantages in obese patients compared to lean diabetics [1,2].

Careful monitoring of blood glucose and HbA1C is an integral component of standard diabetes care. They are designed to assess the effectiveness of a treatment plan and provide guidance in choosing the right medication and dosage. SMBG allows patients to assess their own response to treatment, minimize the risk of hypoglycemia, and determine whether they are gaining glycemic control. Optimal glycemic control is achieved when FPG is 70-130mg/dL, 2 hours post prandial <180mg/dL, and bedtime glucose is 90-150mg/dL. However, testing six to eight times a day can be overwhelming for the patient and may lead to non-adherence. Therefore, it is recommended to ensure that patients are properly instructed and given regular evaluation and follow-up [1,3].

Careful monitoring of blood glucose is especially important in diabetic patients on an intense insulin regimen (three to four injections of basal and prandial pumps or insulin). It monitors and prevents hyperglycemia and possible side effects of hypoglycemia. Blood glucose levels are usually checked before eating, before exercising, before driving, and at bedtime [4].

DISCUSSION

The discovery of biguanides were found to contain guanidine, galegin, and biguanide, which lower blood glucose levels. Metformin is a biguanide which is the primary first-line oral drug of choice in the management of therapy in all age groups. Metformin activates the active protein kinase adenosine monophosphate in the liver, leading to careful hepatic glucose uptake and inhibition of gluconeogenesis through complex effects on mitochondrial enzymes [5].

Metformin is well tolerated and has only mild side effects, a low risk of hypoglycemia and a low likelihood of weight gain. Metformin has been shown to delay the development of diabetes, reduce the risk of complications, and reduce mortality in patients by reducing hepatic glucose synthesis (gluconeogenesis) and insulin-sensitive peripheral tissues. Furthermore, it increases insulin sensitivity by activating insulin receptor expression and increasing tyrosine kinase activity. Recent evidence has also shown that metformin lowers plasma lipid levels via the peroxisome proliferator-activated receptor (PPAR) pathway, which prevents CVD. Metformin is contraindicated in patients with advanced stages of renal insufficiency. If metformin is used when GFR is significantly reduced, the dose should be reduced and the patient should be advised to discontinue treatment if nausea, vomiting, and dehydration arise from other causes (to prevent ketoacidosis) [6,7].

Exenatide and Lira Glutide

Exenatide, an exendin-4 mimetic with 53% sequence homology to GLP-1, is currently approved for treatment as a single drug in the US in combination with metformin ± sulfonylurea. Because of the 2.4-hour half-life, exenatide is recommended for twice-daily dosing. Treatment with exenatide 10g, as an additional add-on to metformin, resulted in significant weight loss (-2.8kg) compared with patients previously treated with metformin alone. Exenatide is generally well tolerated, with mild-to-moderate gastrointestinal effects being the most common side effect [8].

Liraglutide is a GLP-1 analogue that has 97% of the original identity of GLP-1. Liraglutide has a long duration of action (24 hours). Liraglutide caused a 1.5% decrease in A1C in individuals with type 2 diabetes, when used as monotherapy or in combination with one or more oral antidiabetic drugs of choice. Liraglutide for weight loss in diabetic patients. Treatment with liraglutide in combination with a combined metformin/sulphonylurea. Liraglutide also reduces systolic pressure (mean decrease -2.1 to -6.7mmHg). Liraglutide is well tolerated, with only mild nausea and hypoglycemia (risk increases with sulfonylureas). Serum antibody formation was very low in patients treated with once-weekly GLP-1 receptor agonists. The formation of these antibodies does not decrease the efficacy of their action on lowering blood glucose levels [9].

DPP-4 and SGLT-2. Inhibitors

Dipeptidyl peptidase 4 inhibitors include sitagliptin, saxagliptin, vidagliptin, linagliptin, and alogliptin. This drug can be used alone, or in addition to metformin, a sulfonylurea, or a TZD. This treatment is similar to other oral antidiabetic drugs. Gliptins have not been reported to cause a higher hypoglycemic event compared to controls. Dipeptidyl peptidase 4 inhibitors affect postprandial lipase levels.

Treatment with vitagliptin for 4 weeks decreased postprandial plasma triglycerides and the metabolism of triglyceride-rich lipoprotein particles containing 50 triglycerides after a high-fat meal in diabetic patients who had not previously been treated with this drug. In diabetic patients with coronary heart disease, it was shown that treatment with sitagliptin improved cardiac function and coronary artery perfusion. The three most frequently reported adverse reactions in clinical trials with gliptins were nasopharyngitis, upper respiratory tract infection, and headache. Acute pancreatitis was reported in a minority of subjects taking sitagliptin or metformin and sitagliptin.

An increase in the incidence of hypoglycemia was observed in the sulfonylurea treatment group. In the elderly, DPP-4 inhibitors lower blood glucose but have minimal effect on caloric intake and therefore have less catabolic effect on muscle and total body protein mass. In reduced doses, DPP-4 inhibitors are considered safe in patients with moderate to severe renal failure [10].

Sodium-glucose transport inhibitors are a new class of glucosuric agents: canagliflozin, dapagliflozin, and empagliflozin. SGLT2 inhibitors provide insulin-independent glucose reduction by blocking glucose reabsorption in the proximal renal tubule by inhibiting SGLT2. Due to its glucose-free mechanism of action, it may be effective in advanced diabetes when pancreatic -cell reserves are permanently lost. This drug has a weight loss and blood pressure lowering effect. Urinary tract infections leading to urosepsis and pyelonephritis, as well as genital mycoses, may occur with SGLT2 inhibitors. SGLT2 inhibitors rarely cause ketoacidosis. Patients should stop taking their SGLT2 inhibitors and seek medical attention immediately if they have symptoms of ketoacidosis (clear nausea or vomiting, or even non-specific features such as tiredness or abdominal discomfort) [11,12].

Other

Bile acid enzymes: Colesevelam is a bile acid binding resin approved for the treatment of hypercholesterolemia. Can also lower blood glucose and can be used in the treatment of DM. It lowers HbA1c by 0.5% when added to metformin, a sulfonylurea or insulin. The main side effect of colesevelam is relieving constipation. Thus, it should be avoided in patients with gastroparesis or other gastrointestinal motility disorders, in patients following gastrointestinal operative procedures, and in others who are at

risk of obstruction of bowel movements. Other side effects include increased serum triglycerides and possible malabsorption of fat-soluble vitamins [13,14].

Bromocriptine (Cycloset) is a D2 dopamine receptor agonist. FDA approved for the treatment of DM. The dosage range is 1.6-4.8mg, taken with food in the morning within two hours of awakening. It is used as monotherapy or combination therapy with insulin and oral agents and has a good safety profile and tolerability. Its effect on blood glucose may be due to its action on the central nervous system. The mechanism of action of bromocriptine in diabetes has not been clearly elucidated. Side effects include nausea, fatigue, dizziness, orthostatic hypotension, vomiting, and headache. Efficacy in glycemic. Simple control (HbA1c reduction of 0.1-0.4%) [15,16].

CONCLUSION

Inhibitors is for patients not receiving an intensive insulin regimen. According to current guidelines, HbA1C levels should be assessed regularly in all diabetic patients. The frequency of HbA1C testing is flexible and depends primarily on the patient's response to therapy and the physician's judgment. HbA1C testing is performed at least every 6 months for patients who are meeting treatment goals.

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