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Type 2 diabetes mellitus: current diagnosis and treatment

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ABSTRACT

Type 2 diabetes mellitus is a globally prevalent chronic disease caused by obesity, a sedentary lifestyle, hereditary and environmental factors, and multifactorial causes. The prevalence of diabetes has increased worldwide, and its complications cause high morbidity and mortality. With the increase in diabetes and its complications, treatment costs are also increasing. Early diagnosis of type 2 diabetes, timely initiation of treatment, and prevention of complications are crucial. Management of type 2 DM is multifaceted and includes lifestyle changes, pharmacotherapy, and close monitoring of blood glucose levels. In obese individuals, weight loss has been shown to improve glycemic control and reduce the risk of complications. Pharmacologic treatment is tailored to individual needs and may include oral antidiabetic agents, injectable drugs such as insulin, and newer classes of drugs that target specific pathways involved in glucose regulation. Glycemic control is of paramount importance to reduce the risk of microvascular and macrovascular complications associated with T2DM. In conclusion, the diagnosis and treatment of type 2 diabetes require an integrated approach focusing on lifestyle changes, regular follow-up, and personalized pharmacotherapy. Implementing early interventions and maintaining optimal glycemic control are vital to preventing complications and improving the overall condition of individuals with type 2 DM.

Keywords: Type 2 diabetes mellitus, diagnosis, treatment

INTRODUCTION

The prevalence of obesity and the associated prevalence of type 2 diabetes mellitus (type 2 DM) are increasing worldwide. Type 2 DM and obesity are independent risk factors for cardiovascular diseases. Hypertension, dyslipidemia, atherosclerotic heart disease (ASHD), musculoarticular problems, chronic kidney disease (CKD), and peripheral arterial disease are more common in diabetics and obese people. Therefore, diabetes creates a serious financial and moral burden both with its treatment and with the treatment of the complications it brings. Up to 80% of people with type 2 diabetes are obese. When people with a body mass index (BMI) >35 kg/m² were compared with those with a BMI <22 kg/m², the incidence of diabetes was found to increase 80-fold over a 10-year period. In other words, the risk of developing diabetes increases as BMI increases. This shows that in order to achieve lasting success in type 2 DM patients, almost all of whom are obese, perhaps one of the most important goals, besides blood glucose regulation, should be to bring patients to their ideal weight. Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia that develops as a result of peripheral resistance to insulin action, insufficient secretion of insulin, or both. The main clinical symptom of diabetes is hyperglycemia. However, DM is also associated with insulin deficiency and/or insulin resistance, abnormalities in lipid and protein metabolism, and mineral and electrolyte disorders. The International Diabetes Federation (IDF) estimates that the number of type 1 and type 2 diabetic patients worldwide was 463 million in 2019, and this number is estimated to reach 700 million in 2045. The number of type 1 DM patients aged 0-19 years worldwide in 2019 was 1.110.100, and the annual number of new cases was 128.900. In the 2010 TURDEP-II study, the prevalence of DM in Turkey was found to be 13.4%. According to the 2018 Health Statistics Yearbook of the Republic of Turkey Ministry of Health, the prevalence of DM in individuals aged 20-79 years in Turkey was calculated at 12.1%. According to IDF 2019 data, the prevalence of diabetes worldwide is 9.3%.[1-7]

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SYMPTOMS

Diabetes often develops slowly and may not be recognized in its early stages. Common symptoms of diabetes include polyuria, polydipsia, polyphagia, loss of appetite, weakness, fatigue, dry mouth, and frequent nighttime urination (nocturia). Rare symptoms include blurred vision, unexplained rapid weight loss, persistent infections, sores, recurrent infections, numbness, tingling (peripheral neuropathy), and itching. Diabetes can be mildly symptomatic or asymptomatic in its early stages. For this reason, especially at-risk individuals should have regular health checks and examinations for early diagnosis and treatment.[1-3,8-10]

PREDIABETES

Prediabetes refers to a condition prior to the development of diabetes in which blood glucose is higher than normal but does not reach the diagnostic limits for type 2 diabetes. Prediabetes is defined as impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and HbA1c in the range of 5.7-6.4%. It is characterized by increased risk for diabetes and its complications and is characterized by metabolic disorders such as dyslipidemia, physical inactivity, hypertension, obesity, insulin resistance, procoagulant status, oxidative stress, and chronic inflammation. Increased insulin resistance and impaired β-cell function are the most important pathological mechanisms leading to prediabetes and subsequent diabetes. The progression of prediabetes to diabetes can be halted and normoglycemia restored, leading to a reduction in both macrovascular and microvascular complications. Lifestyle changes, a healthy diet, regular physical activity, and weight management play an important role in the prevention and management of prediabetes progression to diabetes. In prediabetes patients with increased insulin resistance, metformin and pioglitazone, which increase insulin sensitivity, may be preferred in medical treatment.[1-3,8,11-14]

DIAGNOSIS OF TYPE 2 DM

The diagnosis of DM is based on plasma glucose (fasting and postprandial) levels, a 75-gram oral glucose tolerance test (OGTT), and HbA1c. If there are no severe symptoms of diabetes, the diagnosis should be confirmed at a later date, preferably with the same method. Impaired fasting glucose (IFG) is defined as fasting plasma glucose (FPG) between 100-125 mg/dl, and impaired glucose intolerance (IGT) is defined as 2nd-hour plasma glucose between 140-199 mg/dl after the oral glucose tolerance test (OGTT). DM is diagnosed if FPG is ≥126 mg/dl, 2nd hour glucose on OGTT is ≥200 mg/dl, or plasma glucose value in randomly drawn blood is ≥200 mg/dl with polyuria, polydipsia, ketonuria, and weight loss.[1-3,12,15-20]

TREATMENT OF TYPE 2 DIABETES

In the treatment of diabetes, where treatment options were limited in the past few years, the options are gradually increasing with the new drugs that are released every day. The treatment of type 2 diabetes should not only be aimed at lowering blood sugar levels; the development of complications should be prevented, and treatment plans should be made for obese diabetics to return to their ideal weight. The patient should be evaluated comprehensively, and treatment should be planned individually. Microvascular complications decrease with lowering HbA1c; however, strict glycemic control has not been proven to prevent macrovascular disease.[1-3,17-19,21]

All patients diagnosed with type 2 diabetes and prediabetes should be counseled about lifestyle changes, including diet and exercise. Many drug options are

Table 1. Antidiabetic drugs

Insulin secretagogues Sulfonylureas Meglitinides
Drugs that increase insulin sensitivity Biguanides Thiazolidinedione derivatives
Alpha glucosidase inhibitors
Sodium glucose co-transporter-2 inhibitors (SGLT2-i)
Insulinomimetic drugs Amylin analogues (pramlintide) Incretin-based treatments [dipeptidyl peptidase 4 (DPP4) inhibitors, glucagon-like peptide 1 (GLP1) analogues]
Insulins Short-acting Intermediate-acting Long-acting Mix insulins

available (Table 1). Metformin is the first choice, unless there is a contraindication. In cases where metformin treatment is not sufficient, a second drug should be selected according to the patient's characteristics. In young patients without comorbidities and complications, the HbA1c target is <7% (or even <6.5%), whereas in elderly patients with multiple comorbidities and limited life expectancy, higher values can be targeted with an HbA1c of 8-8.5%. In elderly patients with a life expectancy of more than 15 years with no comorbidities, the HbA1c target can be set at <7%. In many patients, pharmacologic treatment is initiated if HbA1c >7.5-8% at diagnosis. In patients with HbA1c <7.5%, lifestyle modification can be tried for 3-6 months if the patient is motivated. If HbA1c <8.5%, monotherapy is initiated. Sodium glucose co-transporter-2 (SGLT-2) inhibitors should be considered for patients with cardiovascular risk. If HbA1c is 8.5-10%, double combination is started; if not sufficient, triple combination is planned. Basal or mixed insulin or GLP1 analogs may also be added, and insulin and incretin-based therapies may be an option from the beginning, depending on the patient's characteristics. In patients with high BMI, SGLT-2 inhibitors and GLP1 analogs should be planned to be added to the treatment from the beginning, unless there is a contraindication. If HbA1c is >10%, insulin and/or GLP1 analogs are added to oral therapy.[1-3,16,17,19,21-26]

INSULIN SECRETAGOGUES

Sulfonylureas

They bind to SUR1 receptors in pancreatic beta cells. They increase insulin release from beta cells by inhibiting ATP-dependent potassium channels of the receptor. Beta-cell function is required for them to be effective. These drugs are not effective if C-peptide is severely low in patients who have been followed up for a long time with a diagnosis of diabetes. Today, 2nd-generation sulfonylureas are used. Glibenclamide, Glipizide, Gliclazide, and Glimepiride are commonly used sulfonylureas. Their advantages are that they lower HbA1c by 1-2%, and they are potent and cheap drugs. In the treatment of type 2 diabetes, sulfonylureas can be combined with other oral antidiabetics and insulins; however, they are not given together because they have the same mechanism of action as the meglitinide group. Concomitant use is not recommended when switching to intensified insulin therapy due to the high risk of hypoglycemia. They are effective in patients with maturity-onset diabetes of the young (MODY). The most important side effects are hypoglycemia and weight gain. Patients with irregular diets should be educated about hypoglycemia. They may cause cross-reactions in patients with sulfonamide allergies. They may cause nausea, elevated liver enzymes, and hematologic side effects. They bind tightly to albumin in the circulation and interact with warfarin, sulfonamides, fibrates, and acetaminophen. They may accelerate beta cell loss, and patients' transition time to insulin may be shortened.[1-5,16,21,22,27]

Meglitinides

They bind to a different site of the SUR1 receptor and act through short-term inhibition. They are especially used to lower postprandial blood glucose. They are pharmacologically different from sulfonylureas and can be used in patients with sulfonamide allergies. Meglitinides have a faster onset of action and a shorter duration of action compared to sulfonylureas. Their rapid and short-acting nature allows flexibility in dosing, and the risk of hypoglycemia is lower than with sulfonylureas. Two drugs are available, repaglinide and nateglinide. They are used three times a day, before each meal. Since repaglinide is metabolized by the liver, it can be used in renal failure. It can be given in low doses to patients with a GFR of 20-40 ml/min. It should not be used in patients with a GFR <20 ml/min. Nateglinide undergoes hepatic metabolization, and its renal metabolites are also active. Therefore, caution should be exercised in both renal and hepatic impairment. They cause less hypoglycemia than sulfonylureas and have similar weight-gain effects. Since they bind to the same receptors, concomitant use with sulfonylureas is not recommended.[1-5,16,18,28]

INSULIN SENSITIZERS

Biguanides (Metformin)

Biguanides are widely used in the treatment of type 2 DM. The most widely used first-line treatment is metformin. Biguanides decrease glucose production by the liver, increase glucose sensitivity in cells, and decrease glucose absorption from the intestine. Metformin can be used fast, with or without food; the daily dose is 500-2550 mg (2-3 times a day); the daily dose of metformin in extended-release form is 500-2000 mg (1-2 times a day). It inhibits glucose output from the liver by suppressing gluconeogenesis. The conversion of lactate to pyruvate is also reduced. Metformin also suppresses hepatic gluconeogenesis and lipogenesis by increasing the activation of the AMP protein kinase enzyme. Due to its side effects on the gastrointestinal system and by increasing GLP1 to some extent, it decreases appetite and causes moderate weight loss (0-6 kg). It has cardiovascular protective properties (decrease in total cholesterol, LDL, and VLDL; neutral or increase in HDL; decreases oxidative stress; lowers blood pressure; decreases platelet aggregation). They do not cause hypoglycemia and have their most important

side effects on the gastrointestinal system. Metallic taste in the mouth, loss of appetite, nausea, vomiting, burning in the stomach, bloating, soft stools, and diarrhea occur. Gastrointestinal side effects are less frequent and milder when starting with 500 mg and gradually increasing the dose. A vitamin B12 deficiency may develop. Lactic acidosis may occur, especially in patients with impaired peripheral circulation, heart failure, and severely impaired renal function (9/100.000). Metformin should not be used in shock, hypoxia, COPD, acute decompensated heart failure, and severe renal failure. It should not be started if GFR <45 ml/min; it should be discontinued if GFR <30 ml/min. Contraindications include liver failure, chronic alcoholism, peripheral arterial disease, pregnancy and lactation, major surgical intervention, and advanced age (over 80). It is recommended to discontinue 24 hours before contrast-enhanced procedures (such as angiography, etc.) and restart 24 hours later if creatinine measurement is normal. Can be combined with other diabetes medications and insulins. It does not cause weight gain, hypoglycemia and is inexpensive. It should be continued as long as there are no contraindications.[1-5,16,18,21,29-31]

Thiazolidinedione Derivatives (Pioglitazone)

Glitazones act by increasing insulin sensitivity and decreasing insulin resistance. They decrease glucose production in the liver and increase peripheral insulin sensitivity. It activates peroxisome proliferator-activated receptor (PPAR) gamma. Activation of PPAR-γ increases insulin sensitivity in adipose tissue, skeletal muscle, and the liver. The most commonly used form of glitazone is pioglitazone. The starting dose of pioglitazone is 15-30 mg; the maximum dose is 45 mg, once daily. If edema does not develop for 1-3 months at a low dose and the glycemic response is inadequate, the dose is increased. It has a high effect on reducing HbA1c (0.5-1.4% decrease in HbA1c). It is metabolized in the lung and excreted with bile. They do not cause hypoglycemia, are generally well tolerated, increase HDL levels, decrease triglycerides, reduce secondary cardiovascular events, and lower blood pressure. They reduce insulin resistance by acting primarily on adipose tissue. Benefits have been shown in non-alcoholic fatty liver disease, first choice. They may prevent the progression to diabetes in prediabetics. Glitazones as a group have been shown to significantly reduce the risk of type 2 diabetes, even more so than with metformin. However, despite these findings, the use of glitazones in prediabetic patients is not recommended because the potential side effects such as fluid retention, weight gain, exacerbation of heart failure, osteoporotic fractures, and bladder cancer are greater than the benefits obtained, and the cost of use is quite high. It should not be used in the presence of congestive heart failure (CHF), as it increases sodium reabsorption and associated water retention. The risk of edema is higher in insulin users, women, obese patients, patients with pre-existing edema, and patients with congestive heart failure. Salt restriction is applied, and diuretics are used if necessary. CHF and anasarca edema leading to hospitalization may rarely be seen; they may also cause anemia, weight gain, an increase in liver enzymes, and worsen Graves' ophthalmopathy. May increase the risk of fractures in postmenopausal women and older men and increase respiratory infections. It should not be given to patients with bladder cancer or unexplained hematuria. It is also contraindicated in patients with elevated ALT (if 2.5 times the upper limit of normal), CHF class I-IV according to the New York Heart Association classification, chronic severe renal failure, pregnancy, type 1 DM, risk of macular edema, adolescents, and children.[1-5,7,14,16,21,32]

ALPHA GLUCOSIDASE INHIBITORS

Alpha-glucosidase inhibitors work by slowing down the digestion and absorption of carbohydrates in the small intestine, thus reducing the rise in blood glucose levels after meals. Acarbose is the only agent available in our country, available in 50-100 mg tablets (dosage 50 or 100 mg tablets 3 times a day). The tablets are swallowed with some liquid before a meal or chewed with the first bites during a meal. They inhibit carbohydrate absorption by blocking the breakdown of polysaccharides into monosaccharides in the intestine. Metabolized by intestinal flora, absorption is minimal, and metabolites are inactive. They are weakly effective, reducing HbA1c by 0.5-1.3%. They can provide glycemic control without weight gain, do not cause hypoglycemia, and may prevent the progression to diabetes in prediabetics. Side effects may include bloating, diarrhea, abdominal pain (10-25%) and rarely iron deficiency. Although they do not cause hypoglycemia in monotherapy, they may cause hypoglycemia when used in combination with sulfonylurea, glinide, or insulin. Hepatotoxicity may be seen rarely. The main contraindications include inflammatory bowel disease, chronic ulceration, malabsorption, partial intestinal obstruction, cirrhosis, pregnancy, and lactation.[1-5,33,34]

SODIUM GLUCOSE CO-TRANSPORTER-2 (SGLT-2) INHIBITORS

Sodium-glucose co-transporter-2 (SGLT-2) inhibitors are new-generation oral antidiabetic drugs that have been in use in the treatment of diabetes for the last few years. In Turkey, dapagliflozin, empagliflozin, and the combination of empagliflozin and metformin are available. They have a very important place in

diabetes treatment as they can be combined with all oral antidiabetics, insulins, and GLP1 analogs, and they cause weight loss and hypoglycemia in type 2 DM patients, most of whom are obese. These drugs, called glucoretics or gliflozins, reduce glucose reabsorption in the renal proximal tubules by 30-50% and lower blood glucose levels independently of insulin-mediated mechanisms. In diabetic patients, the reabsorption threshold of the kidney is increased, and renal glucose absorption capacity is increased. This new group of drugs increases glucosuria by inhibiting SGLT-2. Since they act independently of insulin, they can be used in all stages of diabetes. They provide moderate weight loss and, in combination with GLP1 analogs, are the first choice in patients in whom weight loss is desired, unless contraindicated. They have a low risk of hypoglycemia, reduce blood pressure by 2-4 mmHg, and reduce uric acid levels and albuminuria. They reduce cardiovascular mortality, are nephroprotective, and reduce hospitalization for heart failure; therefore, interest in these drugs has increased, and they have started to be used by cardiologists and nephrologists. Phase studies are ongoing in type 1 diabetes but have not yet been approved. They should not be used in ketosis-prone patients because they increase the frequency of ketosis. Side effects include genitourinary infections, fluid loss, dehydration, dizziness, and hypotension. Female patients are more at risk for genitourinary infections. Care should be taken in terms of urosepsis and pyelonephritis. It may cause mild dehydration, and caution should be exercised when used with drugs that may trigger acute kidney injury (such as nonsteroidal anti-inflammatory drugs, ACE inhibitors, angiotensin II receptor blockers, and diuretics). In elderly patients, caution should be exercised in terms of hypotension, dizziness, and falls due to fluid loss, and patients should be informed. If the risk is thought to be high, it should not be given. They increase serum creatinine to some extent; this increase is temporary and may cause a minimal increase in LDL. Euglycemic ketoacidosis may develop; ketones should be checked if nausea and vomiting occur. It should not be started if the GFR is <20 ml/min.[1-5,16,21,22,35,36]

INSULINOMIMETICS DRUGS

Amylin Analogues

Pramlintide is a synthetic analog of amylin. It is used by subcutaneous injection three times a day. It slows gastric emptying, decreases glucagon secretion, and causes weight loss, yet this drug is not available in our country.[1-3]

Incretin Effective Drugs

DPP4 inhibitors: Inhibition of the DPP-4 enzyme, which enables rapid degradation of the GLP-1 molecule in the postprandial period, is a new group of antidiabetic drugs that increases the levels of GLP-1 and GIP, which are endogenous and natural incretins. DPP4 inhibitors, also known as gliptins, increase insulin secretion in a glucose-dependent manner. Sitagliptin, vildagliptin, saxagliptin, linagliptin, and alogliptin are drugs in this group. They decrease glucagon secretion. They are weight-neutral and have no gastrointestinal side effects. Treatment costs are high. They reduce HbA1c by 0.6-1.1%. They can be used in combination with other oral antidiabetics, such as insulin, and may contribute to a reduction in insulin requirement, which indirectly helps the patient lose weight. They can be used in combination with metformin in elderly patients, as the risk of hypoglycemia is higher in the sulfonylurea combination. They have good tolerability, do not cause hypoglycemia, and improve islet cell function by increasing pancreatic alpha and beta cell function. They do not increase the risk of cardiovascular disease. There are data on saxagliptin and alogliptin alone that increase hospitalization for heart failure. The most important side effects are headache, nasopharyngitis, upper respiratory tract infection, gastrointestinal side effects (acute pancreatitis), urinary tract infections, hepatic dysfunction, inflammatory bowel diseases, skin reactions, arthralgia, and myalgia. Linagliptin is eliminated from the enterohepatic system and can be used in chronic renal failure without dose modification. In others, the dose is halved when GFR is <45 ml/min and 75% dose reduction when GFR is <30 ml/min.[1-5,16,21,37]

GLP1 receptor analogues: GLP-1, a member of the family of incretin hormones, is a molecule produced from the intestine that increases insulin secretion from the pancreas in a glucose-dependent manner. This group of drugs, which are GLP-1 receptor agonists, also suppresses glucagon synthesis from alpha cells in the pancreas, slows gastric emptying, and increases the feeling of satiety. Since they act glucose-mediatedly, their hypoglycemia effect is low, and they reduce HbA1c by 0.5-2.5%. Exenatide, liraglutide, lixisenatide, albiglutide, dulaglutide, semaglutide, and tirzepatide are drugs in this group. In addition to the treatment of diabetes mellitus, their use is especially prominent in the treatment of obesity. Favorable effects have been shown in patients at high risk of cardiovascular disease and in patients with nonalcoholic steatohepatitis. Short-acting GLP-1 RAs such as exenatide are more effective on postprandial glucose, allow blood glucose regulation at lower insulin doses, and reduce the weight gain effect of insulin treatment. Liraglutide and semaglutide are used to treat obesity in patients without DM. Relatively longer-acting drugs administered once daily or once weekly have a stronger effect (liraglutide, exenatide XR, dulaglutide, and semaglutide). They are not preferred as

initial treatment because of their high cost, and the fact that they are administered as injections limits their use.

Short-acting exenatide is administered subcutaneously twice a day: liraglutide lixisenatide once a day; albiglutide; dulaglutide; exenatide XR; and semaglutide once a week. In type 2 DM patients with obesity, the use of GLP1 RA in combination with insulin is effective in both sugar regulation and weight loss. Gastrointestinal side effects such as nausea and vomiting are less common when starting with a low dose of the drug, slowly increasing the dose, and achieving tolerance. Cases of pancreatitis and gallstones have been reported with GLP1A drugs, and this group of drugs has been monitored in this respect. If acute pancreatitis is suspected, the drug should be discontinued immediately. It should also be used with caution in patients with a history of gallstones. C-cell hyperplasia in the thyroid has been reported with liraglutide, and further investigation is recommended in the presence of suspected thyroid medullary carcinoma. Worsening of diabetic retinopathy has been reported with semaglutide, and caution is advised in this respect. Exenatide dose reduction is required if eGFR is <30 ml/min/1.73 m^2, while dose reduction is not required for other drugs in this group. Liraglutide has been shown to be useful in diabetic nephropathy. Since GLP1A and dipeptidyl peptidase-4 (DPP4) inhibitors act through the same mechanism, their combined use is not recommended.[1-5,21,24,38-41]

Table 2. GLP1A, half-lives, dosage

	GLP-1RA	Method of Use
Short impact	Exenatide	5-10 mcq / 2 times a day
	Lixisenatide	10-20 µg / once a day
	Liraglutide	0.6-1.8 µg / 1 time a day
Long impact	Dulaglutide	0.75-1.5 µg / once a week
	Semaglutide	0.5-1 mg / once a week
	Exenatide-LAR	2 mg / once a week
	Albiglutide	30-50 µg / once a week

INSULINS

Insulin was discovered in 1921 by Benting and colleagues after long studies. Insulin, which is considered a life-saving treatment, especially in patients with type 1 DM, improves the quality of life in all patients with diabetes. Animal (dog, pig) pancreases were used in the first studies on obtaining insulin. Subsequent and ongoing studies have aimed to increase the effects of insulin, make it more effective for longer periods of time, and use it at the most ideal and stable doses without hypoglycemia. These developments are also factors affecting costs and transportation. Insulin treatment decreases patient compliance due to the difficulties and laboriousness of administration. For this reason, treatment should be planned taking into account the patient's compliance with treatment, and the choice of treatment should be based on the patient's age, comorbidities, presence of diabetic complications, risk of hypoglycemia, work, and daily routine. Insulin therapy is applied to patients with insulin deficiency or who require insulin support.

Indications for insulin therapy; patients with type 1 diabetes mellitus, patients with type 2 diabetes mellitus (HbA1c above 10), pregnancy and lactation, emergency hyperglycemic conditions (diabetic ketoacidosis and hyperglycemic hyperosmolar state) who cannot achieve sugar regulation with non-insulin anti-hyperglycemic therapy, the presence of severe hyperglycemic symptoms, acute coronary syndrome, allergy to non-insulin agents, severe hepatic-renal failure, major surgical operations, acute febrile and systemic disease.

Human insulin and insulin analogs developed by recombinant DNA techniques are used in treatment. Insulin is usually administered subcutaneously.

Insulins are grouped as very fast acting, fast acting, short acting, intermediate acting, long acting, and very long acting. Their onset of action and duration of action are important in the organization of treatment. Prandial (short-, fast-, and very fast-acting) and basal insulin (intermediate-, long-, and very long-acting) use

Table 3. Commonly used insulins

Insulin type	Impact Initiation	Peak time	Duration of impact
Lispro, Aspart, Glulisin	3-15 min	45-75 min	2-4 hours
Regular	30 min	2-4 hours	5-8 hours
NPH	2 hours	4-12 hours	8-18 hours
NPA/Asp 70/30	6-12 min	1-4 hours	18-24 hours
Insulin glarjin	2 hours	Peakless	24 hours
Insulin detemir	2 hours	3-9 hours	6-24 hours*
Insulin glarjin U300	2 hours	Peakless	<36 hours
Insulin degludek	2 hours	Peakless	>40 hours
Insulin deg/Asp 70/30	14-72 min	2-3 hours	>24 hours

suppresses gluconeogenesis and ketogenesis and corrects hyperglycemia. In addition to long-acting insulins, long-acting concentrated insulins have been developed for use in patients who are regulated with high doses of insulin. Fast-short-acting insulins can be used intramuscularly (i.m.) and intravenously (i.v.), but i.m. and i.v. use of medium-long-acting insulins is contraindicated. The types of insulins and their modes of action are given in Table 3.

Insulin is usually administered subcutaneously, and the rate of absorption is affected by ambient temperature (faster in heat, slower in cold) and injection site (from fast to slow; abdomen, arm, thigh, buttock). During insulin therapy, complications such as hypoglycemia, an increase in body weight, edema, immunogenicity (the development of antibodies against insulin preparations), lipohypertrophy and atrophy at the injection site, bleeding, oozing, and pain may occur. In patients with type 2 diabetes, if adequate blood glucose regulation cannot be achieved with oral anti-diabetic therapy, basal insulin (0.1-0.2 U/kg) or NPH is added once daily. Basal insulins are preferred over NPH because they are longer-acting and cause less hypoglycemia. When basal insulin is not sufficient, twice-daily mixed insulin or basal-bolus therapy may be administered. Ready-made combinations of basal insulin and GLP1 analogs are also a form of treatment administered once daily, with dose titration based on basal insulin dose and fasting blood glucose. Basal-bolus (multiple dose) treatment is administered to patients with type 1 diabetes, pregnant patients who cannot be regulated despite diet, and patients with type 2 diabetes who cannot be adequately regulated with other treatments. Fast-short-acting insulin (bolus) is administered 3 times a day before meals and medium-long-acting insulin (basal) 1-2 times a day. The physical activity, body mass index, presence of diabetic complications, and previous insulin use determine the insulin requirement. A maintenance dose of 0.4-1.0 IU/kg/day is required in type 1 diabetics and 0.3-1.2 IU/kg/day in type 2 diabetics. In basal-bolus insulin treatments, approximately half of the total daily insulin requirement is basal, and the remaining half is bolus. Fast-acting insulins can be used 5 minutes before a meal, short-acting insulins 15 minutes before a meal, and very fast-acting insulins with a meal.[1-5,42-44]

CONCLUSION

The prevalence of obesity and type 2 DM is increasing. Treatment is individualized; an appropriate treatment approach should be chosen for each patient, and weight reduction treatment should be prioritized in obese patients.

ETHICAL DECLARATIONS

Referee Evaluation Process: Externally peer-reviewed.

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