EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 10
Issue: 1
192-199
Year: 2023

DIABETES: TYPES, RISK FACTORS AND TREATMENT- A REVIEW

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Article Received on 08/11/2022 **Article Revised on 29/11/2022** **Article Accepted on 19/12/2022**

ABSTRACT
Diabetes mellitus is group of metabolic disorders that affect utilization of glucose in body and this glucose is important source of energy for the cells. Diabetes mellitus is characterized by hyperglycemia as body is unable to take up glucose to use it for energy production resulting in increased blood sugar level. This may happen due to defects in production of insulin, action of insulin or combination of both. This article discusses the different types, risk factors for diabetes and treatment options for diabetic patients.

KEYWORDS: Diabetes mellitus, insulin, hyperglycemia, metabolic disorder.

INTRODUCTION

Diabetes mellitus is group of metabolic disorders and is characterized by hyperglycemia due to defects in production of insulin, action of insulin or combination of both. Chronic Diabetic hyperglycemia results in long term damage, dysfunction and failure of some organs such as eyes, kidneys, nerves, heart and blood vessels.[1]

Diabetes mellitus word is taken from Greek word diabetes which means siphon- to pass through and the Latin word mellitus which means sweet. The term diabetes was first used by Apollonius of Memphis around 250 to 300 BC. Sweet nature of urine in diabetes was observed by Ancient Greek, Indian and Egyptian civilizations, hence diabetes mellitus word came into existence. In 1889, Mering and Murkowski, found the role of the pancreas in the pathogenesis of diabetes. Banting, Best, and Collip in 1922, purified the insulin from the pancreas of cows at the University of Toronto, and made available as an effective treatment for diabetes in 1922. Over the years, exceptional work, and multiple discoveries, as well as management strategies, have been introduced to manage this emerging problem. Unfortunately, even today, diabetes is one of the most common chronic diseases in the worldwide. In the US, it remains as the seventh leading cause of death.[2]

All countries, irrespective of their economic development, epidemiological and demographical variations among these countries, are facing an increasing burden of non-communicable diseases including diabetes mellitus. Non-communicable diseases (NCDs) are becoming main health problems with continually increasing burden. Diabetes mellitus is one major segment of these chronic non-communicable diseases. In 2000, 60% of deaths in the world were due to NCDs. International Diabetes Federation (IDF), reported that approximately 75–80% of people with diabetes mellitus die due to cardiovascular complications.[3]

Previous literature around the world found variation in the level of the prevalence of diabetes mellitus. In Guatemala, the prevalence of diabetes found was 8.4% where almost half of them (4.1%) were newly reported. In Bangladesh, an increased prevalence of diabetes was reported among females, old age, centrally obese and urban dweller. In Korea it was reported that 21.8% and 15.3% of participants had impaired fasting glucose level and diabetes respectively. The World Health Organization (WHO) found prevalence of diabetes in Kenya will rise from 3.3% in 2000 to 4.5% by 2025. In African countries the prevalence of diabetes mellitus type 2 ranged from 1% in rural Ugandato 12% in urban Kenya. WHO reported that in Ethiopia about 800,000 people having diabetes in year 2000 and the number is expected to increase to 1.8 million by the year 2030.

A community-based study in Gondar reported that the prevalence of diabetes mellitus among adults of age 35 years and above was 3.6%, while prevalence was 5.1% for urban and 2.1% for rural people. Most of cases (69%) of diabetes were newly diagnosed; with the highest proportion (82.6%) in rural residents.[4-8]

Classification of Diabetes mellitus

Classify diabetic patients is not an easy task as many patients do not fit easily into a single class of diabetes

classification. It was observed that 10 % patients those were initially classified may need revision later on. American Diabetes Association (ADA) gave the classical classification in 1997 as type 1, type 2, other types, and gestational diabetes mellitus (GDM) and it is still the most accepted classification and adopted by ADA.

Type 1 diabetes mellitus

This is autoimmune type which is due damage of β cells of the pancreas. The hallmark of type 1 diabetes is the presence of autoantibodies against the pancreatic islet cells, although the contribution of these antibodies in the pathogenesis of the disease is not clear. These autoantibodies include islet cell autoantibodies and autoantibodies to insulin, glutamic acid decarboxylase (GAD, GAD65), protein tyrosine phosphatase (IA2 and IA2β) and zinc transporter protein (ZnT8A). These pancreatic autoantibodies are main feature of type 1 diabetes and could be detected in the serum of patients with this type of diabetes months or years before the onset of the disease. This autoimmune type 1diabetes has strong HLA associations, with linkage to *DR* and *DQ* genes. This autoimmune type 1 diabetes is featured by the absence of insulin secretion and is predominantly found in children and adolescents.[9]

The rate of β-cell damage is variable, this damage is rapid in some individuals, mainly infants and children but slow in adults. In some patients, especially children and adolescents, ketoacidosis is the first manifestation of the disease. Other patients have modest fasting hyperglycemia which can rapidly convert to severe hyperglycemia and/or ketoacidosis in the presence of infection or stress. Other patient mainly adults, may have preserved residual β-cell function which is sufficient to prevent ketoacidosis for many years. Such patients become insulin dependent for their survival and are at risk for ketoacidosis. At this latter stage of the disease, there is little or no insulin secretion, as manifested by low or undetectable levels of plasma C-peptide. Immune-mediated diabetes commonly occurs in childhood and adolescence, but it can occur at any age, even in the 8th and 9th decades of life.[2]

Type 2 diabetes mellitus

Type 2 diabetes mellitus accounts for ~90–95% of patients those with diabetes. Previously it was referred to as non–insulin-dependent diabetes or adult-onset diabetes. Individuals with this type of diabetes have insulin resistance and usually have relative insulin deficiency. At initial stages, and also throughout life time, these patients do not need insulin treatment for their survival. Although the specific etiological factors are not known, but there are probably various etiological factors causing this type of diabetes. Autoimmune destruction of β-cells does not occur in these patients.[2]

Most patients with this type of diabetes are obese, and this obesity of patient results in some degree of insulin resistance in these patients. Patients who are not obese may have an increased percentage of body fat distributed predominantly in the abdominal area. Ketoacidosis in these patients seldom occur spontaneously; But when occurs, it usually occurs in association with the stress of another disease or infection.[2]

Gestational diabetes: This type of diabetes develops in some females during their pregnancy. This Gestational diabetes usually goes away after pregnancy.

There are two classes of this diabetes. Class A1 in which women can manage it through diet and exercise. Class A2 diabetic women need to take insulin or other medications for management.

Gestational diabetes goes away after birth of baby. But it can affect baby's health.[11] However, if a woman has gestational diabetes, she is at higher risk of developing Type 2 diabetes later on in life.[10]

Women with gestational diabetes usually don't have symptoms. Mostly it is diagnosed during a routine screening.

One may notice that:

- More Thirstier than normal
- More hungrier and eat more than usual
- Patient pee more than usual

During pregnancy, placenta makes hormones that cause glucose to build up in blood. Usually, pancreas can send out enough insulin to manage it. But if body can't make enough insulin or stops using insulin as it should, blood sugar levels increase, and female develop gestational diabetes.[11]

Risk factors for diabetes mellitus

Risk factors for Type 1 diabetes include

- Patients having a family history of Type 1 diabetes.
- Injury to the pancreas such as by infection, tumor, surgery or accident.
- Presence of autoantibodies.
- Physical stress such as surgery or illness.
- Exposure to illnesses caused by any virus.

Risk factors for prediabetes and Type 2 diabetes include

- Family history of Type 2 diabetes.
- Having overweight/obesity.
- Having high blood pressure.
- Having low HDL cholesterol and high triglyceride level.
- Being physically inactive.
- Being age 45 or older.
- Having gestational diabetes or giving birth to a baby weighing more than 9 pounds.
- Having polycystic ovary syndrome.
- Having a history of heart disease or stroke.
- Being a smoker.[10]

Gestational Diabetes Risk Factors

- Overweight before pregnancy
- Women Have blood sugar levels that are higher than they should be but not high enough to be diabetes.
- Have a family member suffering from diabetes
- Women have had gestational diabetes earlier.
- Females with polycystic ovary syndrome (PCOS) or another health condition linked to problems with insulin.
- Females having high blood pressure, high cholesterol, heart disease, or other medical complications.
- Women, who gave birth to a large baby weighing more than 9 pounds.
- Women who have given birth to a stillborn baby or had some birth defects
- Are older than 25 years.[11]

Tests for type 1 and type 2 diabetes and prediabetes

***Glycated hemoglobin (A1C) test*:** This blood test doesn't need not eating for a period of time (fasting) and it depicts average blood sugar level for the past 2 to 3 months. It gives the percentage of blood sugar attached to hemoglobin which is oxygen-carrying protein in red blood cells. The higher the blood sugar levels, the more hemoglobin present with sugar attached. An A1C level of 6.5% or higher on two separate tests means that you have diabetes. An A1C between 5.7% and 6.4% means that you have prediabetes. Below 5.7% is considered normal.

Random blood sugar test: A blood sample will be taken at a random time period. No matter when you last ate, a blood sugar level of 200 milligrams per deciliter (mg/dL) — 11.1 millimoles per liter (mmol/L) — or higher suggests diabetes.

Fasting blood sugar test: A blood sample will be taken after you haven't eaten anything the night before (fast). A fasting blood sugar level less than 100 mg/dL is considered as normal. A fasting blood sugar level from 100 to 125 mg/dL is taken as prediabetes. If it's 126 mg/dL (7mmol/L) or more than this on two separate tests, patient has diabetes.

Oral glucose tolerance test: For this test, patient has to fast overnight. Then, the fasting blood sugar level is measured. Then patient is asked to drink a sugary liquid, and blood sugar levels are tested regularly for the next two hours. A blood sugar level less than 140 mg/dL (7.8 mmol/L) is considered as normal. Blood sugar level of more than 200 mg/dL (11.1 mmol/L) after two hours means patient is diabetic. A reading between 140 and 199 mg/dL means patient has prediabetes.[12]

Management of Diabetes mellitus

The goal of diabetes treatment is to maintain blood glucose levels as close to normal level as safely possible. As in patients with diabetes, there may be increased risk for heart disease and peripheral artery disease, measures to control blood pressure and cholesterol levels are major part of diabetes management.

People with diabetes must be responsible for their routine care. This includes monitoring blood glucose levels, dietary management, maintaining physical exercise, keeping weight and stress under control, monitoring oral medications and, if required, insulin use via injections or pump.

When opting appropriate pharmacologic therapy, it is necessary to determine whether the patient is insulin-deficient, insulin-resistant, or both. Diabetes management options are divided into insulin therapy and noninsulin therapy which includes insulin sensitizers, secretagogues, alpha-glucosidase inhibitors, incretins, pramlintide, bromocriptine, and sodium-glucose cotransporter 2 (SGLT-2) inhibitors.[13]

Insulin therapy

Patients with type I diabetes need to take insulin as their body does not make it. There are different methods to take insulin. It can be taken by using a needle and syringe, an insulin pen or by an insulin pump. An artificial pancreas, also referred as automated insulin delivery system, may be used as an alternative for some patients.[14]

There are different forms of insulin are available. Each type of insulin starts to work at a different speed, called as “onset,” and effects of each type of insulin last a different length of time, known as “duration.” Most types of insulin have the strongest effect when they reach a peak. After the peak, the effects of the insulin wear off over the next few hours or so.[14]

Table 1: Types of insulin and how they work.[15,16]

Insulin Type	How Fast It Starts to Work (onset)	When It Peaks	How Long It Lasts (duration)
rapid-acting/ ultra rapid-acting	15 minutes	1 hour	2 to 4 hours (rapid) 5 to 7 hours (ultra)
rapid-acting, inhaled	10 to 15 minutes	30 minutes	3 hours
regular, also called short-acting	30 minutes	2 to 3 hours	3 to 6 hours
intermediate-acting	2 to 4 hours	4 to 12 hours	12 to 18 hours
long-acting	2 hours	does not peak	24 hours
ultra long-acting	6 hours	does not peak	36 hours or longer

Premixed insulin is a combination of insulins listed in above Table. Premixed insulin begins to work in 15 to 60 minutes and it can last from 10 to 16 hours. The peak time is variable which depends on the type of insulins are mixed.

Insulin injections

Patient can take insulin shots using a needle and syringe after taking dose of insulin from the vial—or bottle—through the needle into the syringe. Insulin works fastest when it is injected in the belly. Injecting insulin in the same spot repeatedly could make the tissue harden, so it is difficult to take shots in that area over time. Other spots where insulin can be injected include thigh, buttocks, or upper arm, but it may take longer time for the insulin to work when injected in those areas. Some patients with diabetes who take insulin need 2 to 4 shots a day to reach their blood glucose targets and others need to take a single shot.[14]

Insulin Pens

They are available in different shapes and use an insulin cartridge instead as opposed to a vial. Some insulin pens have replaceable cartridges and other insulin pens use non replaceable cartridges and these pens should be disposed of after their use. The replaceable cartridges for insulin pens available in different sizes that are 3 and 1 ½ ml. Size 3 is more common and has become dominant. Prefilled insulin pens are disposed of when the insulin within the cartridge is used up. Prefilled pens are often marketed for type 2 diabetics patients who need to use insulin.[17]

Insulin pens are easier to use, but they are more costly than needles and syringes. Some patients use an insulin pen as they find it hard to fill the syringe while holding the vial or cannot read the markings present on the syringe. Different pen types have features that can help the patients for their injections. Some reusable insulin pens have a memory function, due to which it can recall dose amounts and timing. Other types of insulin pens which can be programmed to calculate insulin doses and provide downloadable data reports.[14]

Insulin pump

It is a small machine which gives the steady doses of insulin throughout the day. Patient can wear one type of pump outside the body on a belt or in a pocket or pouch and it delivers insulin into the layer of fat that is just below the skin. This insulin pump is connected to a small plastic tube and a very small needle. Patient insert the plastic tube with a needle under skin, then take out the needle. The plastic tube will stay inserted for several days while attached to the insulin pump. The machine pumps insulin through the tube into the body 24 hours a day and it can be programmed to provide more or less insulin depending on patient's needs. Doses of insulin can be given through the pump at mealtimes. An insulin pump consists of the main pump unit which holds an insulin reservoir which typically holds between 176 and 300 units of insulin.

Second type of pump attaches directly to skin with a self-adhesive pad and is controlled by a hand-held device. The plastic tube and pump device are changed every several days.[14,17]

Jet injector

It is a device which gives a fine spray of insulin into the skin at high pressure instead of using a needle to deliver the insulin. This jet injector is used less commonly than a needle and syringe or a pen.[14]

Inhaler

Insulin can be taken by breathing powdered insulin into mouth from an inhaler device. The inhaled insulin goes into lungs and quickly enters into blood.[14]

Insulin inhalation is used in combination with long-acting insulin to manage type 1 diabetes and also used in combination with other medications to treat patients with type 2 diabetes who need insulin to control their diabetes. Insulin inhalation is not used for the management of diabetic ketoacidosis. Insulin inhalation is a short-acting, man-made alternative of human insulin and it works by replacing the insulin which is normally produced by the body. It helps to move sugar from the blood into other body tissues where it is used for energy and it also stops the liver from producing more sugar, thus controlling the blood sugar level.[18]

This therapy may decrease the chances of having some complication related to diabetes such as heart attack, stroke, kidney failure, nerve damage, eye problems, including changes or loss of vision, or gum disease.

Insulin inhalation may cause side effects. These are:

- Cough
- Sore throat or irritation
- Tiredness
- Diarrhea
- Nausea
- Headache
- Painful, burning urination
- Weight gain

Insulin inhalation is used at beginning of each meal. Proper directions on prescription label should be followed and take it exactly as directed. Never take more or less dose than prescribed by the physician. This therapy controls diabetes but it does not cure it. So do not stop using it without doctor's consultation.

Basal-bolus injection regimen

This regimen involves taking a number of injections through the day including injection at each meal. This therapy may be given to patients with type 1 and type 2 diabetes. This regimen involves taking a longer acting form of insulin to maintain blood glucose levels stable

through the periods of fasting and separate shorter acting insulin injections to prevent rises in blood glucose levels resulting from meals.

Basal insulin keeps blood glucose levels under control, and allows the cells to take in glucose for energy. It is usually taken once or twice a day depending on the insulin. It is usually long acting or intermediate type.

A bolus dose is insulin that is specifically taken at meal times to maintain blood glucose levels following a meal. Bolus insulin needs to act fastly. Therefore short acting insulin or rapid acting insulin is used as bolus insulin. Bolus insulin is often taken before meals but sometimes, it may be advised to take insulin during or just after a meal to prevent hypoglycemia.

A basal-bolus regimen is popular amongst people with diabetes, particularly for working adults who may need to be flexible with when they take their doses and how much carbohydrate they eat.

Patient with type 1 diabetes take rapid acting insulin at meal times and long acting insulin once or twice a day.

Patients with type 2 diabetes may be prescribed with a basal-bolus regimen if they experience significantly high blood glucose levels after their meals and need to have a flexible insulin regimen to fit in with their routine life.

Patient with type 2 diabetes may take a combination of short acting and intermediate insulin, or may take rapid acting and long acting insulin.

Blood glucose testing for a basal-bolus regimen

People taking a basal-bolus regimen will need to regularly examine their blood glucose levels through the day to check whether the correct doses are being taken.

Hypoglycemia can be a relatively common occurrence in patients taking a basal-bolus regimen so it is advised to keep blood glucose testing kit and a source of fast acting carbohydrate in conditions when blood glucose levels go too low.[19]

Advantages of a basal-bolus regimen

- Basal-bolus regimen allows fairly closely match how patient's own body would release insulin if it was able to.
- It also allows for flexibility as to when meals are taken.
- If patient is self-adjusting his/her insulin doses, it means they have flexibility for taking amount of carbohydrates in different meals.

Disadvantages of a basal-bolus regimen

- This regimen involves taking more insulin injections each day that may more problematic in some patients than others.[19]

Non-Insulin Therapy

Insulin Sensitizers

Insulin sensitizers decrease glycemic load mainly by improving action of insulin in peripheral tissues. There are two classes of these oral hypoglycemic drugs which are available: biguanides and thiazolidinediones. They have been shown in clinical use and have positive, durable effects in the management of diabetes mellitus. These drugs can be used as monotherapy or in combination with other medications such as sulfonylurea, insulin, or with each other.

Biguanides (Metformin)

Metformin is the only biguanide drug that was first marketed in the 1950s. Since then, many metformin products have been approved by the FDA, both generic and proprietary. The primary mechanism of action of this drug is suppression of hepatic glucose output, but it also increases insulin sensitivity of muscle and fat. Metformin mainly decreases fasting glycemia but some of them reduce postprandial glucose concentrations, especially after the mid day meal.

Metformin is well tolerated by patients and its most common side effect is gastrointestinal (GI) complaints that include diarrhea, nausea, and abdominal discomfort, and a metallic taste. These symptoms improve with time and dose reduction. Metformin also brings a small increase in basal and postprandial lactate concentrations in the blood that can result in rare but life-threatening lactic acidosis.[20,21] So it is better to avoid metformin use in patients with hepatic impairment. Metformin is also contraindicated in male patients with a serum creatinine level of 1.5 mg/dL or more and in females with a level of 1.4 mg/dL or higher.[21]

The main benefit of metformin is that its use usually does not result hypoglycemia when it is used as monotherapy. Its use can result in weight loss, and it has been shown to reduce plasma triglycerides concentration by 10% to 20%.[21]

Metformin dose is usually taken twice daily, but it can be dosed 3 times daily. Its extended-release formulation is taken once daily. The typical starting dose of metformin is 500 mg/day with a maximum dose of 2,550 mg/day. To prevent GI complications it is gradually started at 500 mg with breakfast and increasing its amount by 500 mg in weekly intervals until reaching a maximum dose of 1,000 mg with breakfast and dinner.[21,22]

Thiazolidinediones

There are two thiazolidinediones which are marketed: rosiglitazone and pioglitazone. Generic products are available for both these drugs. These are agonists of peroxisome proliferator-activated receptor gamma. They mainly increase sensitivity of muscle and fat, and, mildly, the liver, to exogenous and endogenous insulin. All these effects decrease fasting and postprandial blood glucose levels.

Main side effects of these drugs include weight gain, with an increased subcutaneous adiposity and fluid retention, which lead to peripheral edema although heart failure has occurred occasionally. These side effects mostly occur at higher doses of medication. Therefore, these drugs should be avoided in patients with functional class III or IV heart failure.

The Prospective Pioglitazone Clinical Trial in Macrovascular Events showed that when it is compared with placebo, does not increase cardiovascular risks.[23] The thiazolidinediones have been linked with an increased risk of bone fractures, especially in women. They do not result in hypoglycemia when used as monotherapy. Pioglitazone use can also decrease triglycerides, increase high-density lipoprotein (HDL), and increase the low-density lipoprotein particle size.

It is taken as one dose once daily. Thiazolidinediones become fully effective in 2 to 12 weeks. For rosiglitazone, the starting dose is 4 mg/day and maximum dose of 8 mg/day. For pioglitazone, the starting dose is 15 mg/day and the highest dose is 45 mg/day.[7]

Insulin Secretagogues

These trigger secretion of insulin from the pancreas, thereby increasing glucose uptake by muscles and fat and reducing hepatic glucose production. Two types of secretagogues are available which are: sulfonylureas and glinides.

Sulfonylureas

These drugs were first introduced for the treatment of type 2 diabetes in the mid-1950s. Till 994, these were the only oral drugs available in the United States. These agents act by binding to a regulatory protein on pancreatic β-cells, which in turn, leads to closure of ATP-dependent potassium (K_{ATP}) channels resulting in membrane depolarization and influx of calcium through voltage-dependent channels, which subsequently results in insulin secretion.[23]

Glinides

There are two drugs available in these classes which are: Nateglinide and repaglinide. These drugs have same mode of action as sulfonylureas but glinides have a more rapid onset of action and act for a shorter duration, so these drugs are a good alternative for patients with erratic timing of meals. The hypoglycemia risk with these drugs is less than with sulfonylureas but there is a similar-to-lower risk of weight gain after initiating therapy with glinides. Precaution must be taken when it is used in patients with liver dysfunction.

Alpha-Glucosidase Inhibitors

This drug class act by competitively blocking the enzyme alpha glucosidase in the brush borders of the small intestine, which leads to delay in absorption of carbohydrates. Their main target is postprandial hyperglycemia but do it without causing hypoglycemia. GI complaints include bloating, abdominal cramps, flatulence, and diarrhea. Use of these drugs should be avoided in patients with severe hepatic or renal impairment. Dosing of these drugs must occur before carbohydrate-containing meals.

Incretins

Incretin-based therapy is available as injections (glucagon-like peptide-1 [GLP-1] receptor agonists) or oral preparations (dipeptidyl peptidase-4 [DPP-4] inhibitors). These therapies are different slightly in their mechanisms of actions. All incretin-based drugs carry a higher risk of acute pancreatitis. Patients must be aware about this risk and be advised to stop taking these drugs and go for medical consultation if acute abdominal pain develops.

These drugs should not be given to patients who have a history of medullary thyroid carcinomas or have multiple endocrine neoplasia type 2. They increased the incidences of thyroid C-cell tumors in murine models. So far, no increased risk in humans has been reported.[24]

DPP-4 inhibitors

These drugs may help in weight loss as well as reduce blood glucose levels, but have been associated with increased rates of pancreatitis.

Drugs in this class

This drug class includes medications:

- Januvia (Sitagliptin)
- Galvus (Vildagliptin)
- Onglyza (Saxagliptin)
- Tradjenta (Linagliptin) – approved for use in the USA

These drugs act by blocking the action of DPP-4, an enzyme which destroys a group of gastrointestinal hormones called incretins.

Incretins hormones help in stimulation of insulin production when it is needed and decrease the production of glucagon by the liver when it is not needed. They also decrease the digestion and reduce appetite. Therefore DPP-4 inhibitors protect incretins from destruction and help in regulation of blood glucose levels.

DPP-4 inhibitors may be used as a second or third line treatment for patient with type 2 diabetes after prescribing metformin and sulphonylureas, and as an alternative to thiazolidinedione drug.

Benefits of gliptins

As these are effective in reducing blood glucose levels and also they can help in reduction of appetite, therefore they may be beneficial for patient needs to lose weight.

Adverse effects of DPP-4 inhibitors include:

- Gastrointestinal problems – including nausea, diarrhoea and stomach pain
- Flu-like symptoms such as headache, runny nose, sore throat
- Skin reactions that are painful skin followed by a red or purple rash[25]

Pramlintide

The human hormone amylin is insoluble and has a tendency to self-aggregate, which makes it difficult to use therapeutically. To overcome this problem, a soluble, non-aggregating, equipotent analog of human amylin, pramlintide, was prepared.

Subcutaneous meal time injections of pramlintide have been evaluated as a alternative method to replace or supplement amylin in diabetic patients who need insulin. Pramlintide doses of 60 to 120 µg in patients with diabetes result in plasma concentrations of pramlintide that mimic physiological postprandial concentrations of amylin in subjects without diabetes mellitus. After a single subcutaneous injection of this medication, plasma concentrations reach to peak at about 20 minutes and then decrease during the next 3 hours. Pramlintide is excreted by the kidneys, with little or no hepatic metabolism. Plasma half-life of pramlintide is 50 minutes.

Clinical evaluations reported that uses of pramlintide have shown decrease in postprandial glucose concentrations through at least three distinct mechanisms of action, which are: slowing of gastric emptying, prevention of the postprandial increase in plasma glucagon, and increased satiety, resulting in reduced caloric intake and potential weight loss.

Patients with diabetes mellitus often have accelerated gastric emptying than healthy subjects. This may be due to deficient amylin secretion in response to meals, among other factors. Because gastric emptying is a physiological influence for glucose entering the circulation, accelerated gastric emptying may exacerbate postprandial glucose excursions in patients with diabetes mellitus. As Pramlintide slow down the gastric emptying, controlling the rate at which nutrients are delivered from the stomach to the small intestine and, consequently, the rate at which glucose enters the circulation after meals. This effect leads to a decreased postprandial glucose excursion without changing the net absorption of ingested carbohydrate or other nutrients.[26]

CONCLUSION

Improper treatment of diabetes can result in serious problems, causing damage to various organs of body such as heart, kidney, eyes and nerves. Therefore it is necessary to make proper diagnosis for diabetic condition of patient so that appropriate treatment option can be selected based on the type of diabetes. The earlier diabetic condition is diagnosed, sooner the treatment can be started to manage it as if blood sugar level is maintained, and the patient is more likely to live a long and healthy life.

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