



International Journal of Medicine and Pharmaceutical Research

Journal Home Page: www.pharmaresearchlibrary.com/ijmpr



Review Article

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A Review on Newer Trends in Treatment for Diabetes Management in Health Care Practice

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ABSTRACT

It is a group of metabolic diseases in which there is high blood sugar levels over a prolonged period. Diabetes is due to pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. Type 1 DM results from the pancreas failure to produce enough insulin. Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood-sugar levels. The patients having the symptoms of polyuria, ployphasia, polydypsia, vision loss, leg ulcers. Diabetes is the leading cause of ESRD because diabetic nephropathy develops in 30 to 40% of patients. The progression of diabetes results in nephropathy, neurological manifestations, optic nerve damage. We conclude that early detection and diagnosis educating the patients about disease regular monitoring of blood sugar levels, Pharmacotherapy keeps the diabetes in control. We hope that newer trends for diabetes treatment like stem cell therapy, gene replacement therapy, cells replacement therapy have been introduced. Approaching these trends minimizing the diabetes complications in the society.

Keywords: Ulcers, beta cells, ESRD, insulin, pancreas, stem cells.

ARTICLE INFO

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Article History: Received 28 April 2016, Accepted 27 May 2016, Available Online 10 June 2016

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Manuscript ID: IJMPR2983



PAPER-QR CODE

Citation: A. Bharath Kumar, et al. A Review on Newer Trends in Treatment for Diabetes Management in Health Care Practice. *Int. J. Med. Pharm. Res.*, 2016, 4(3): 174-178.

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1. Introduction

Diabetes mellitus is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin [1] produced. Type 1 DM results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown. Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood-sugar levels. Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas, leading to insulin deficiency [2]. The majority of type 1 diabetes is of the immune-mediated nature, in which a T-cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin. Type 1 diabetes is partly inherited, with multiple genes, including certain HLA genotypes, known to influence the risk of diabetes [3].

2. Type 2 DM

Type 2 DM is characterized by insulin resistance, which may be combined with relatively reduction in insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor [4]. At this stage, high blood sugar can be reversed by a variety of measures and medications that improve insulin sensitivity and reduction in the liver's glucose production. It happens due to modified lifestyle factors and genetics. It includes obesity, body mass index of greater than 30, lack of physical activity, poor diet, and stress. The patient is consuming sugar-sweetened drinks in excess is associated with an increased risk [5].

Gestational diabetes

It involves a combination of relatively inadequate insulin secretion and responsiveness. It can Management through modified dietary changes, blood glucose monitoring is required.

Pre diabetes

Pre-diabetes indicates a condition that occurs when a person's blood glucose levels are higher than normal but not high enough for a diagnosis of type 2 DM [6].

History of Diabetes from Ancient to Modern Era

Diabetes is one of the first diseases described in Egyptian manuscripts in 1500 BCE mentioning "too great emptying of the urine. The team of Indian physicians identified as disease and classified as madhumeha or honey that tempts the urine would attract ants. The term "diabetes" or "to pass through" was first used in 250 BCE by the Greek Apollonius of Memphis. Type 1 and type 2 diabetes were identified as different conditions in practice. The first time by the Indian physicians Sushruta and Charaka in 400-500 CE with type 1 associated with youth and type 2 with obesity. The term "mellitus" or "from honey" was added by Thomas Willis in the late 1600s and the other condition like diabetes insipidus which is also associated with frequent urination. In medieval Persia, Avicenna (980–1037) International Journal of Medicine and Pharmaceutical Research

provided information in the Canon of Medicine, "described as the abnormal appetite associate with sweet taste of diabetic. In 1776 Matthew Dobson confirmed that the sweet taste comes from an excess of a kind of sugar in the urine and blood. In 1910, Sir Edward Albert Sharpey-Schafer suggested that people with diabetes having deficiency in chemical that was normally produced by the pancreas [12]. He proposed as substance insulin, from the Latin insula, meaning island, in reference to the insulin-producing islets of Langerhans in the pancreas. The endocrine role of the pancreas in metabolism, and indeed the existence of insulin, was further clarified in 1921, when Sir Frederick Grant Banting and Charles Herbert Best demonstrated they could reverse induced diabetes in dogs by giving them an extract from the pancreatic islets of Langerhans of healthy dogs. The islets of Langerhans was discovered in 1869 by an anatomist named Paul Langerhans. He identified the keys cells in the pancreas which produce the main substance that controls glucose levels in the body. This led to the availability of an effective treatment insulin injections and the first patient was treated in 1922. The researches makes effective in Insulin production and therapy rapidly spreaded around the world. The November 14 considered as a World Diabetes Day towards honor of scientist banting and best.

Other landmark discoveries for insulin include:

- Development of the long acting insulin like NPH in the 1940s by Novo-Nordi.
- Identification of the first of the sulfonylureas in 1942.
- Reintroduction of the use of biguanides for Type 2 diabetes in the late 1950s.
- The phenformin metformin was first marketed in 1979-1994 in the US.
- The radioimmunoassay for insulin, as discovered by Rosalyn Yalow and Solomon Berson (gaining Yalow the 1977 Nobel Prize in Physiology or Medicine)[12]
- The three-dimensional structure of insulin was developed.
- Identification of the first thiazolidinedione in 1990s.
- In 1980, U.S. biotech company Genentech developed biosynthetic human insulin.
- In india 1996 effective insulin researches developed through biotechnology approaches.

Risk factors for development of type 2 diabetes

- Obesity
- Lack of physical activity.
- History of gestational diabetes.
- Impaired glucose tolerance.
- Impaired fasting glucose.
- Drug therapy - combined use of a thiazide diuretic with a beta-blocker.
- Low-fibre diet
- Metabolic syndromes.
- Polycystic ovarian syndrome.
- Family history (2.4-fold increased risk for type 2 diabetes).

The following matter represents causes of diabetes:

- Genetic defects of β -cell function

- Maturity onset diabetes of the young
- Mitochondrial DNA mutations.
- Genetic defects in insulin processing or insulin action
- Defects in pro insulin conversion
- Insulin gene mutations
- Insulin receptor mutations

Exocrine Pancreatic Defects

- Chronic pancreatitis
- Pancreatectomy
- Pancreatic neoplasia
- Cystic fibrosis
- Hemochromatosis
- Fibrocalculous, pancreatopathy

Drugs

- Glucocorticoids
- Thyroid hormone
- -adrenergic agonists Statins

Endocrinopathies

- Growth hormone excess Cushing syndrome
- Hyperthyroidism Pheochromocytoma.

Infections

- Cytomegalovirus infection, Coxsackievirus B

3. Pathophysiology

The generation of glucose from non-sugar substrates in the body. Insulin plays a key role in balancing glucose levels in the body. It can inhibit the breakdown of glycogen or the process of gluconeogenesis and stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen [7]. Insulin is released into the blood by beta cells (-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. Then finally elevated levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as acidosis [8].

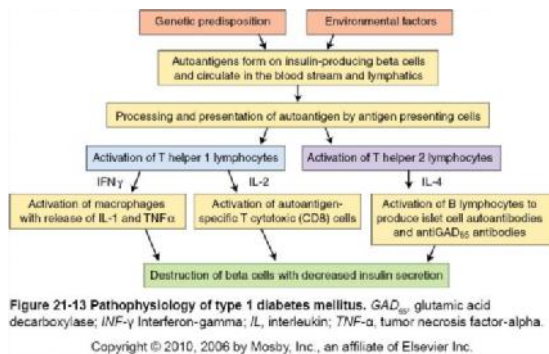


Figure 1: Pathophysiology of Diabetes

4. Epidemiology

In 2013, 382 million people have diabetes worldwide. This is equal to 8.3% of the adult population with equal rates in

both women and men. In 2014, the International Diabetes Federation (IDF) estimated that diabetes resulted in 4.9 million deaths. The World Health Organization (WHO) estimated that diabetes resulted in 1.5 million deaths in 2012, making it the 8th leading cause of death. The higher in status was expected to occur in Asia and Africa, where most people with diabetes will probably live in 2030[9].

Clinical symptoms of diabetic patients

Being excessively thirsty, feeling tired, always feeling hungry, having cuts that heal slowly, itching, skin infections, blurred vision, gradually putting on weight, mood swings, headaches, feeling dizzy, leg cramps [10].



Figure 2: Clinical symptoms of diabetic patients

Counselling and life style modifications for diabetic patients: Counselling regarding the disease:

We need to educate the diabetic patients on disease and modifications in the lifestyle pattern. They should also stress upon the importance of Pharmacotherapy if they were neglected the disease may affect the quality of life. The pharmacist should focus on the key practice areas including diet, exercise, smoking and alcohol intake.

A. Diet: the dietary counseling, importance should be given for the dietary content including carbohydrate, fat and fiber intake.

1. **Carbohydrates:** Most young people will require 180 g of carbohydrate per day, whereas 100 g may suffice for an elderly patient. If fiber rich food such as whole meal bread, jacket potatoes, etc. are eaten, then the carbohydrate content of the diet make up to 50% to 55% of the calories.
2. **Fat:** Educating the diabetic patient restriction in consumption of fatty foods. The high fat foods results in progression of coronary disease.
3. **Fiber:** Dietary fiber has two useful properties. Firstly, it is physically bulky and increases satiety. Secondly, fiber delays the digestion and absorption of complex carbohydrates, thereby minimizing hyperglycemia.
4. **Exercise and physical activity:** Exercise can help to promote weight loss and maintain ideal body weight when combined with restricted caloric intake.
5. **Alcohol intake:** The modest amount of alcohol will alter blood glucose levels.
6. **Smoking:** People with diabetes, especially those over age 40 years, who smoke and have high blood

pressure and cholesterol, are at a higher risk for cardiovascular problems. When the large blood vessels (arteries) are blocked, heart attack and stroke often result.

- This will hardening or blockage may also occur in the small arteries that supply blood to the legs and feet.
- It leads to serious complications like infections, ulcers, gangrene, and even amputations.

Oral hypoglycemic agents (OHAs) therapy for diabetes management

Some general approaches to be followed for patients receiving OHAs: The patient should be strictly cautioned with not to skip meals at any time and to follow regular eating patterns to prevent hypoglycemia. OHAs are comparatively safe drugs [12]. However some patients may develop loss of appetite, nausea and vomiting, abdominal pain, cramps, malaise, diarrhea or weight loss while using OHA's.

Table 1: Oral hypoglycemic agents and its effects

Drugs	Administration time	Dosing schedule	Possible side effects	Comments
Glibenclamide	Taken with meal or 15 to 30 mins before food.	Usually taken in one or two doses	Hypoglycemia, obesity	Interacts with Oral anticoagulants
Glimperide	Taken with meal	Usually taken in a single dose	Hypoglycemia	Interacts with Oral anticoagulants
Gliclazide	Taken with meal	Usually taken in one or two doses	Hypoglycemia	Interacts with Oral anticoagulants
Glipizide	Taken with meal	Usually taken in one or two doses	Hypoglycemia	Interacts with Oral anticoagulants
Metformin	Take during or immediately after a meal to minimize gastrointestinal side effects.	Usually taken in one to three doses	GI disturbances	Should be stopped before surgery and radiological investigations involving contrast media
Acarbose	Swallow whole with liquid before meal or chew with the first few mouthfuls of food.	Usually taken in one to three doses	GI disturbances	Sucrose should not be administered if the patient experience hypoglycemia
Repaglinide	Taken with meal	Usually taken three times in a day	Hypoglycemia	-
Pioglitazone	Taken with meal	Usually taken in a single dose	Hypoglycemia	-

Diabetes associated health complications [4]

- Diabetic neuropathy:** It is characterized by nerve damage caused by chronic high blood glucose levels. Neuropathy can lead to loss of pain or touch sensations on the feet. It can causes pain in legs, arms or hands. Nerve damage can progress slowly and most of the time the patients may not even be aware that they have nerve problems.
- We have to advise the patients restriction in usage of limiting alcohol intake, smoking consumption.
- Diabetic retinopathy:** Retinopathy is a disorder of the eye that occurs in majority of the adults with diabetes. The patient suffering from retinopathy may complain of blurring of vision, seeing black spots, flashing light.
- Diabetic nephropathy:** Nephropathy (disorder of the kidney) is one of the potential life threatening complications of diabetes. Poor control of diabetes is associated with enlargement of the kidneys and impairment in their function.
- Infections:** Many infections we can see commonly in diabetic patients. Infections at mild

stages, if not treated, can lead to develop septicemia, leg ulcers, and wounds in epithelial surface.

- Cardiovascular disease.
- Foot damage.
- Hearing impairment.
- Alzheimer's disease.

Insulin: There are wide varieties of insulin preparations available in the market. It may differ in source, onset of action, time to peak effect, and duration of action.

Table 2: Counseling points for insulin

Steps	Counseling points
Drawing of insulin from the vial	Draw air into the syringe in an amount corresponding to the prescribed amount of insulin. Inject the air into the vial. Invert the vial and draw up insulin little more than prescribed amount. Hold the vial vertically at eye level. Inject the excess amount of insulin, together with any air bubbles, back into the vial. Pull out the needle.
Site of self injection	The best sites for self injection are the front and outer sides of the thigh, and the abdomen.
Injection techniques	Clean the injection site with spirit. Pinch the skin at the injection site in a broad fold and insert the needle at an angle of 45 degrees into the subcutaneous tissue. Inject the insulin slowly. Then press your finger against the injection site while pulling out the needle.
Rotating the injection site	Rotate the injection site in the chosen area so as not to injure the tissue beneath the skin.
Disposal of the needles	Disposable syringes must be discarded, so that they do not cause harm to others. Glass and metal syringes have to be thoroughly cleaned before every use.
Time of administration	The patient should be advised to administer the insulin as per the doctor's advice. In general insulin preparations should be taken 30 mins before food.
Storage of insulin	Insulin should be stored at a temperature of 2-8 degrees Centigrade. In case the patient doesn't have a refrigerator he can be advised to put the vial in a glass of water. The patient can be also advised to have thermostat bags that can retain the stability of the preparation.
Adverse drug reactions	Advise the patient to monitor for allergic reactions (especially with bovine/porcine insulin) and also for hypoglycemia.
Specialized devices in administering insulin	Insulin pen has several advantages (easy to carry, less pain and accurate dose administration). Suitable candidates for insulin pen should be isolated and advised by the pharmacist.

Newer trends for diabetes treatment in health care practice: Gene Therapy

Through this approach introduction of a foreign gene into any cell type in the body, allowing it to stimulate release of insulin. The gene introduced could be the insulin gene itself, perhaps under control of a tissue-specific promoter, allowing for expression in a select non- cell type, or a gene encoding a factor that in turn activates the insulin gene, thereby allowing for insulin production [11, 13].

Cell-replacement therapy

The cells origin from -cell and immortalized to allowing for unlimited expansion in culture or non- cells manipulated to produce insulin [10, 13].

Stem cell therapy for diabetes management

The Mesenchymal stem cells in patients with diabetes type 2 leads to increased development of new vascular pattern, stimulation of immune protective systems and up regulation of pancreatic transcription factors and vascular growth factors results in insulin secretion. It creates a micro-environment which supports beta cell/resident stem cell activation and surveillance. Through this approaches using individual own stem cells [6] can help the pancreas regenerate and strengthen its ability to stimulate and release insulin.

5. Conclusion

We conclude that Diabetes is a chronic illness that prevention requires both pharmacological and non-pharmacological measures for better control. Educating the Patients about complications of diabetes and adherence to medications, an insulin therapy and lifestyle modification plays a crucial role in diabetes management in the

community. Through this approaches we can minimize the progression of its complications in general health care practice.

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