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REVIEW ARTICLE

RISK FACTORS MANAGEMENT AND RECENT ADVANCES IN TREATMENT OF DIABETES

Meshram P. V. *, Moregaonkar S. D., Tripathi S. D., Ambade R. B., Shirale S. Y. and Masare P. S.

Bombay Veterinary College, Parel, Mumbai-12,
Maharashtra Animal and Fisheries Sciences University, Nagpur, India

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Abstract: *Diabetes mellitus is a metabolic disorder characterised by resistance to the action of insulin, insufficient insulin secretion, or both. Once it was regarded as a single disease entity, now seen as a heterogeneous group of disease, characterized by a state of chronic hyperglycaemia resulting from a diversity of aetiologies like environmental and genetic makeup acting jointly. The clinical manifestation of diabetes mellitus is hyperglycaemia, altered metabolism of lipids, carbohydrates and proteins with an increased risk of vascular complications. Worldwide, diabetes represents a rapidly growing problem and affects about 180 million people across the globe and the figure is expected to increase to 366 million by 2030. For better management of risk factors and treatment of short-term as well as long-term diabetes related problems, emphasis should be given on nutritional support, glucose monitoring programme, as well as long-term glycaemic control.With the progress of biomedical sciences and technology, lot of advancement in the treatment of diabetes was took place. Recent advancements like, Pancreas transplantation, Islet cell transplantation, artificial pancreas, Stem cell approach, Gene therapy approach and Nanotechnology are upfront. Recent advancement of these therapies approaches and understanding of risk factors involvedhelps in a better management of diabetes and complications thereof.*

Key wards: *Diabetes mellitus, management, recent advancement, hyperglycaemia, blood glucose, insulin.Pancreas transplantation, Gene therapy, Nano-technology.*

Introduction:

The term **Diabetes,** coined by Aretaeus of Cappadocia, is derived from the Greek word, "*diabainein*" that literally means "passing through, or siphon", isreferenced to excessive urine production. Later, the Latin term **Mellitus** (sweetened or honey like) was added based on its taste. Actually, diabetes mellitus is a heterogeneous chronic metabolic disorder, accompanied with disturbances of carbohydrate, fat and protein metabolism with hyperglycaemia resulting from defect in insulin secretions. It is clinically exhibited by symptoms such as weakness, polyuria, polydipsia, polyphagia, ketonemia, ketonuria and causes complications to the eyes, kidneys, and nerves. It is also associated with an increased incidence of cardiovascular disease **(Pickup and Williams, 1991).**

The high blood glucose levels in diabetes is either due to less production of insulin by the pancreas or due to inability of body cells to respond to the insulin produced. Based on this, there are two types of diabetes: Type I and Type II. Type I is also called as insulin-dependent diabetes mellitus (IDDM) which is mainly due to less production of insulin and type II as non-insulin-dependent diabetes mellitus (NIDDM) which is mainly due to inability of body cells to respond to the insulin produced **(WHO, 2013).**

Diabetes is majorly classified into diabetes mellitus and diabetes insipidus. Diabetes insipidus is characterized by the persistent excretion of excessive quantities of dilute urine and by thirst because of deficiency of production of anti-diuretic hormone (ADH), a hormone secreted by posterior pituitary gland. Characteristically, diabetes is a long term disease with variable clinical manifestations and progression **(WHO, 1980).**

Types of Diabetes:

The first widely accepted classification of diabetes was published by the WHO in 1980 (Second

Report, 1980). Two major classes of diabetes mellitus were proposed: IDDM (Type I) and NIDDM (Type II). Gestational diabetes as well as other types was also included. The modified form of 1985 (Diabetes Mellitus: Report of a WHO Study Group, 1985) was widely accepted and is used internationally. The terms Type I and Type II were introduced to describe the cases which are primarily due to pancreatic islet beta-cell destruction the former and the common major form of diabetes resulting from defects in insulin secretion the latter **(Goodpaster *et al.*, 2010).**

Cause(s) of Diabetes:

Diabetes is basically caused, either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. It's overall due to complex mechanism of gluconeogenesis.

Blood glucose is tightly regulated by homeostatic mechanisms and maintained within a narrow range in circulation. A balance is preserved between the entry of glucose into the circulation from the liver, supplemented by intestinal absorption after meals and glucose uptake by peripheral tissues, particularly skeletal muscle. A continuous supply of glucose is essential for the brain which uses glucose as its principal metabolic fuel. When intestinal glucose absorption declines between meals, hepatic glucose output is increased in response to the counter-regulatory hormones glucagon and adrenaline, and it falls during prolonged starvation as other metabolic fuels derived from fat become more important. The liver produces glucose by gluconeogenesis and glycogen breakdown. Insulin is the only anabolic hormone that has profound effects on the metabolism of carbohydrates, fat and protein. Disturbances in insulin secretion ultimately results in diabetes mellitus **(Frier *et al.*, 2010).**

Risk Factors for Diabetes:

There are controllable risk factors associated with diabetes, including obesity and an inactive lifestyle. However, other uncontrollable risk factors, such as ethnicity, age, family history and genetics, also play a dramatic role.The primary risk factor for type I diabetes is a family history of this lifelong, chronic disease. Having family members with diabetes is a major risk factor. The American Diabetes Association (Standards of medical care in diabetes-2007) recommends that anyone with a first-degree relative with type I diabetes a mother, father, sister, or brother should get screened for diabetes. A simple blood test can diagnose Type I diabetes. In addition, injury or diseases of the pancreas can inhibit its ability to produce insulin and lead to type I diabetes. A range of relatively rare infections and illnesses can damage the pancreas and cause Type I diabetes **(Stamler 1993).**

The risk factors associated with type II diabetes include obesity, diet and physical inactivity, increasing age, insulin resistance, family history of diabetes, genetic factors, race and ethnicity. As concerns genetic factors, research has shown that certain gene variations raise the risk of developing diabetes. These genes can be associated with insulin sensitivity in the body's tissues, decreased insulin production and an increased risk of obesity. Race and ethnicity, on the other hand, are responsible for higher levels of diabetes in certain ethnic groups including African Americans, Mexican Americans, American Indians, native Hawaiians and some Asian Americans. The above mentioned groups have an increased risk of diabetes and heart disease. This is partly due to higher rates of high blood pressure, obesity and diabetes in these populations **(Boulton *et al*, 2005)** however, the detailed research on these factors to cause diabetes in animals are still awaited.

Clinical Signs, Symptoms and Diagnosisof Diabetes:

Polyuria, polydipsia and polyphagia are the classical triad of diabetes symptoms. These symptoms may develop quite fast in type I, particularly in children but may be subtle or completely absent as well as developing much more slowly in type II diabetes. In type I, there may also be weight loss (despite normal or increased eating) and irreducible fatigue. Those symptoms may also manifest in type II diabetes also whose diabetes is poorly controlled.

Thirst develop because of osmotic effects sufficiently high glucose (above the renal threshold) in the blood is excreted by the kidneys, but this requires water to carry it and causes increased fluid loss, which must be replaced. The lost blood volume will be replaced from water held inside body cells, causing dehydration. Prolonged high blood glucose causes changes in the shape of the lens in the eye, leading to vision changes. Blurred vision is a common complaint leading to a diagnosis of type I **(Alberti andZimmet, 1998).**

Risk Factor Management and Treatment of Diabetes:

For better management of risk factors and treatment of short-term as well as long-term diabetes related problems, emphasis should be given on patient education, nutritional support, self-glucose monitoring, as well as long-term glycaemic control. A scrupulous control is needed to help reduce the risk of long term complications. In addition, given the associated higher risks of cardiovascular disease, lifestyle modifications must be implemented to control blood pressure and cholesterol by exercising more and consuming an appropriate diet **(Susman and Helseth, 1997).**

Management of Diabetes without Drugs:

Exercise, Weight and Diet control play an important role in management of diabetes.

Exercise: Regular exercise is of particular importance for diabetics. It ultimately helps you to keep your blood sugars within a normal range. By exercising, the cells in the body help to make insulin more effective because it makes the body's cells more sensitive to insulin. Patients with type 1 or type II diabetes have an increased risk of coronary artery disease. Physical exercise is a key component of lifestyle modification that can help individuals prevent or control type II diabetes. Although diet is probably more important in the initial phases of weight loss, incorporating exercise as part of a weight loss regimen helps maintain weight loss and prevent weight regain. Mild to moderate activity levels have been associated with a lower risk of developing diabetes or pre-diabetes. 30 minutes of moderate physical activity daily may offer protection from diabetes. The studies indicate that exercise should be a mainstay of primary prevention of diabetes **(Michael, 2007; Stewart, 2008).**

Weight: It can be important factor in diabetics because it can make one's body become resistant to insulin. Exercise helps to keep weight down because calories are burned when one exercises. If fewer calories are consumed than one can burn, weight can be lost. A recent study demonstrated that both women and men who have a BMI > 35 kg/ m 2 had a 20-fold increase in their risk of developing diabetes compared to people with a BMI of 18.5 - 24.9 kg/m 2. Obese people also have a high incidence of hypertension and hyperlipidemia compared to no obese people, which may further increase their risk of microvascular and macrovascular complications of diabetes. Weight loss also has been shown to decrease systolic and diastolic blood pressure and LDL cholesterol and lipid levels in obese diabetic patients.

Diet: The diet plays a tremendous role in the management of diabetes because it is important to keep the blood sugar within a normal range. Substantial dietary restriction to 1,100 kcal/day has been shown to decrease fasting blood glucose of patients with diabetes and even in those without diabetes in, as few as 4 days (**Michael, 2007; Kirkwood, 2007).**

a. **Carbohydrates:** Carbohydrates are the body's main source of energy. Starches and sugars are carbohydrates and they are both broken down into glucose at approximately the same speed. Sweet foods can cause diabetes Carbohydrates raise the blood sugar much more rapidly than fats and proteins and must be avoided in diabetes (**Beaser, 1995).**
b. **Protein:** The body uses protein as the second major nutrient to build body tissue as well as repair body tissue. Proteins consist of foods such as meats, eggs, cheese, peanut butter etc. The best sources of protein are those that are low in fat, such as lean meat and skinless poultry. Proteins contain enzymes. Some

enzymes are responsible for breaking down starches into sugars. Proteins also slow the release of sugars into the bloodstream leading to aggravate diabetes. **(Michael, 2007)**.

c. **Fat:** The third major nutrient needed by the body is fat. Fats are important because they carry fatty acids and vitamins in the body. It can be found in such things as cheese, margarine, butter, meat, milk, and vegetable oils. All fats are high in calories. Fats, like proteins, facilitate the release of sugars into the bloodstream. Because saturated fats are the major dietary determinants of serum LDL cholesterol levels. Cholesterol consumption should be <200 mg/ day. Being a diabetic does not mean that one has to give up all of the foods that we enjoy, but we have to pay particularly close attention to the meals that we eat. **(Michael, 2007).**

Allopathic Treatment of Diabetes Mellitus:

Conventional treatment of diabetes in allopathic medicinal system revolves around the use of following drugs **(Tripathi *et al*, 2006).**

a. Insulins: Rapid acting, Short acting, Intermediate acting, Long acting
b. Sulfonylureas: First generation, Second generation
c. Biguanides
d. Meglitinide/Phenylalanine analogues
e. Thiazolidinediones
f. Glucosidase Inhibitors

Recent Advances in Treatment of Diabetes:

With the progress of biomedical sciences and technology, lot of advancement in the treatment of diabetes was took place. Advancements like, Pancreas transplantation, Islet cell transplantation, Artificial pancreas, Stem cell approach, Gene therapy approach and Nanotechnology are upfront.

a. Pancreas transplantation:

A pancreas transplant is an organ transplant that involves implanting a healthy pancreas (one that can produce insulin) into a person who usually has diabetes. Because the pancreas is a vital organ, performing functions necessary in the digestion process, the recipient's native pancreas is left in place, and the donated pancreas is attached in a different location. In the event of rejection of the new pancreas, which would quickly cause life-threatening diabetes, there would be a significant chance the recipient would not survive very well for long without the native pancreas, however dysfunctional, still in place. The healthy pancreas comes from a donor who has just died or it may be a partial pancreas from a living donor.

The prognosis after pancreas transplantation is very good. Over the recent years, long-term success has improved and risks have decreased. One year after transplantation more than 95% of all patients are still alive and 80-85% of all pancreases are still functional. After transplantation patients need lifelong immunosuppression. Immunosuppression increases the risk for a number of different kinds of infection and cancer **(Fishman and Rubin, 1998).**

b. Islet cell transplantation:

Highly used approach in humans to cure type I diabetes. Islets cells are injected into the patients liver, where they begin to produce insulin. The islet cells seem to produce insulin well in that environment. The patient's body treats the new cells just as it would do to any other foreign body. The immune system will attack the cells as it would do to a bacterial infection. Thus, the patient also needs to undergo treatment involving immune suppression, which reduces immune system activity **(Robertson, 1999).**

c. Artificial pancreas:

Artificial pancreas involves implantation of bio-engineered tissue containing islet cells, which would secrete the amounts of insulin, amylin and glucagon needed in response to glucose.

d. Stem cell approach:

Islet cells are developed from stem cells taken from umbilical cord blood of newborn babies

e. Gene therapy approach

Gene therapy can be used to manufacture insulin directly, consisting of viral vectors containing the insulin sequence, is digested and delivers its genes

to the upper intestines. Those intestinal cells will then behave like any viral infected cell and will reproduce the insulin protein. The virus can be controlled to infect only the cells which respond to the presence of glucose, such that insulin is produced only in the presence of high glucose levels. Gene therapy is also used to cure patients having ß cell destruction. It is also used to turn duodenum cells into ß cells, which produce insulin and amylin. Naturally ß cells will produce insulin in proportional response to carbohydrates consumed **(Welsh, 1999;**

f. Nano-technology approach:

To cure diabetes type I patients many nanobots are injected into the patients' blood stream. These nanobots synthesize insulin and secrete it according to the level of glucose they would sense **(Yamaoka, 2001).**

References:

Alberti, K. G. and P. Z. Zimmet (1998) Definition diagnosis and classification of diabetes mellitus and its complications. Part I: Diagnosis and classification of diabetes mellitus, provisional report of a WHO consultation. Diabetes Med, 15: 539-553.

Beaser, R. and J. Hill (1995) A Program for Managing your treatment: The Joslin Guide to Diabetes. New York: A Fireside Book: By Simon and Schuster.

Boulton, A.J., A. I. Vinik, J. C. Arezzo, V. Bril, E.I. Feldman, R. Freeman, R.A. Malik, R. E. Maser, J. M. Sosenko and D. Ziegler (2005) Diabeticneuropathies: a statement by the American Diabetes Association. Diabetes Care, 28:956-962.

Fishman, J. A. and R.H. Rubin (1998) "Infection in organ-transplant recipients". N Engl J Med. 338 (24): 1741–51.

Frier, B. M. and M. Fisher (2010) Diabetes Mellitus: In Nicki R, Brian R, Stuart H, editors. Davidson□s Principle and Practice of Medicine, 21st edition. Elsevier;.India, pp.735-745.

Goodpaster, B. and A. Detany (2010) Effect of diet and physical activity interventions in severely obese adults: a randomized trial. JAMA, 304 (16):17951802.

Kirkwood, L. (2007) Effects of advice on dietary intake and/or physical activity on body composition, blood lipids and insulin resistance following a low-fat, sucrose-containing, high carbohydrate, energy-restricted diet. IntJ of Food Sci&Nutr, 58 (5); 383-397.

Michael, J. F. (2007) Diabetes Treatment, Part 1: Diet and Exercise. Clin Diabetes, 25(3): 105-109.

Pickup, J. C. and G. Williams (1991) Classification and diagnosis of diabetes mellitus and impaired glucose tolerance. In: Textbook of diabetes, Volume 2 Blackwell Scientific Publications, London, UK. 37-44.

Robertson, R. Paul (1999). Pancreas and islets transplants for patients with diabetes: Taking positions and making decisions. Endocrine Practice, 5(1): 2428.

Stamler, J. (1993) Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. Diabetes Care, 16: 434-444. Laakso

Stewart, M. and A. Swtsinger (2008). Exercise can help control diabetes. Herald and Review (Decatur, IL).

Suman, J. L. and L. D. Helseth (1997) Reducing the complications of type II diabetes: a patient centered approach. Am. Fam. Physician, 56: 471-80.

Tripathi, B. K. and A. K. Srivastava (2006) Diabetes mellitus: Complications and therapeutics. Medical Science Monitor 12(7): RA130-147.

Welsh, N. (1999) Gene therapy in Diabetes mellitus: promises and pitfalls. CurrOpinMolTher ,1: 464-470.

WHO, (1980) Expert committee on diabetes mellitus. Second report. Technical report series 12, Genewa, pp.646,

WHO, (2013) "Diabetes Fact sheet No.312 (www.who.int/mediacentre/factsheets/fs312/en/)

Yamaoka, T. (2001) Gene therapy for Diabetes mellitus. Current, Mol Med,1(3): 325-337.