Complications of diabetes mellitus

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Abstract

Diabetes mellitus is a chronic metabolic disorder, which is characterised by chronic hyperglycaemia and disturbances of carbohydrate, protein and fat metabolism, resulting from defects in insulin secretion, insulin action or both. The long-term effects of diabetes include the development of retinopathy, neuropathy and nephropathy. People with diabetes are also at increased risk of other diseases, including cardiac, cerebrovascular and peripheral arterial disease. Other long-term complications of diabetes include digestive problems, skin problems, sexual dysfunction and problems with the gums and teeth. Numerous factors, in addition to directly related medical complications, contribute to the impact of diabetes on quality of life and economics. Diabetes is associated with a high prevalence of depression, and adversely impacts employment, absenteeism and work productivity. With the correct treatment and recommended lifestyle changes, many people with diabetes are able to prevent or delay the onset of possible complications.

Introduction

Diabetes refers to a group of diseases which affect how the body uses blood sugar (glucose). Glucose is vital to health because it is an important source of energy for the cells which comprise the muscles and tissues. It is also the brain’s main source of fuel. Diabetes causes blood glucose to become too high.¹ Several pathogenic processes are involved in the development of diabetes. These include processes which impair or destroy the function of the pancreatic beta cells, with consequent insulin deficiency; and others which result in resistance to insulin action, e.g. insulin resistance and insulin insensitivity. Abnormalities of carbohydrate, fat and protein metabolism are due to the deficient action of insulin on the target tissues, resulting from insensitivity to, or lack of, insulin, or both.²

Symptoms

Patients with diabetes may present with the following characteristic signs and symptoms, which include:³¹

- Increased thirst
- Frequent urination
- Extreme hunger
- Unexplained weight loss
- The presence of ketones in the urine. (Ketones are a byproduct of the breakdown of muscle and fat which occurs when not enough insulin is available)
- Fatigue
- Irritability
- Blurred vision
- Slow-healing sores

- Frequent infections, such as gum or skin infections, and vaginal infections.

The most severe clinical manifestation is ketoacidosis or nonketotic hyperosmolar state, which leads to stupor, coma, and in the absence of treatment, death.²

What complications are associated with diabetes?

People with diabetes have an increased risk of developing a number of serious health problems. Consistently high blood glucose levels lead to serious diseases which affect the heart, blood vessels, eyes, kidneys, nerves and teeth. Diabetes is a leading cause of cardiovascular disease, blindness, kidney failure and lower limb amputation in almost all high-income countries.⁴⁶

These complications develop over many years, and they all relate to how blood glucose levels affect the blood vessels. Over time, high blood glucose damages the body’s blood vessels. Damaged blood vessels don’t deliver blood as well as they should. Type 2 diabetes affects the large blood vessels, causing plaque to eventually build up, and potentially leading to a heart attack, stroke or vessel blockage in the legs (peripheral vascular disease).⁷⁹

Maintaining blood glucose levels, blood pressure and cholesterol at, or close to, normal, helps to delay or prevent diabetes complications. Therefore, people with diabetes need regular monitoring.⁵ Patients with diabetes require ongoing evaluation for diabetes-related complications. A history and physical examination should be performed 2–3 times yearly, to obtain information on nutrition, physical activity, the management of diabetes and cardiovascular risk factors, as well as diabetes-related complications.⁵
Long-term complications of diabetes develop gradually. The longer the duration of diabetes and the less controlled the blood sugar, the higher the risk of complications. Eventually, diabetes complications are disabling or even life-threatening. Possible complications are now discussed.

**Cardiovascular disease**

Cardiovascular disease affects the heart and blood vessels, and causes complications such as coronary artery disease, leading to a heart attack, and strokes. Cardiovascular disease is the most common cause of death in people with diabetes. High blood pressure, high cholesterol, high blood glucose and other risk factors contribute to an increased risk of cardiovascular complications.5,6

Diabetics have a 1.5 times higher risk of having a stroke than people who do not have diabetes. A stroke occurs when the blood supply to part of the brain is suddenly interrupted. Most strokes occur because a blood clot blocks a blood vessel in the brain or neck. A stroke causes movement problems, pain, numbness and problems with thinking, remembering or speaking. Some people also have emotional problems, such as depression, after a stroke.4,6

**Diabetic neuropathy**

Nerve damage from diabetes is called diabetic neuropathy. Approximately half of all people with diabetes have some form of nerve damage. It is more common in those who have had the disease for a number of years.4 Excess glucose injures the walls of the tiny blood vessels (capillaries) which nourish the nerves, especially in the legs. This causes tingling, numbness, burning or pain which usually begins at the tips of the toes or fingers and gradually spreads upwards. Left untreated, all sense of feeling in the affected limbs is lost. Damage to the nerves relating to digestion causes problems with nausea, vomiting, diarrhoea or constipation. It leads to erectile dysfunction in men.1,6

**Diabetic nephropathy**

The kidneys contain glomeruli that filter waste from the blood. Diabetes damages this delicate filtering system.7 Kidney disease is caused by damage to the small blood vessels in the kidneys, leading to the kidneys becoming less efficient or failing altogether. Kidney disease is much more common in people with diabetes than in those without it. Maintaining near-normal levels of blood glucose and blood pressure greatly reduces the risk of kidney disease.5 Severe damage leads to kidney failure or irreversible end-stage kidney disease, for which dialysis or a kidney transplant is required.1

**Diabetic ketoacidosis**

Diabetic ketoacidosis is a serious condition which can lead to diabetic coma, or even death. When the cells don't receive the glucose they need for energy, the body begins to burn fat for energy, which produces ketones. Ketones are chemicals which the body creates when it breaks down fat to use for energy. The body does this when it doesn't have enough insulin to use glucose, the body's normal source of energy. When ketones build up in the blood, they make it more acidic. They are a warning sign that the diabetes is out of control.4

**Eye complications**

Most people with diabetes develop some form of eye disease (retinopathy), which causes reduced vision or blindness. Consistently high levels of blood glucose, together with high blood pressure and high cholesterol, are the main causes of retinopathy.5,7

People with diabetes are 40% more likely to suffer from glaucoma than people without it. Glaucoma is more common the longer someone has diabetes. The risk also increases with age. Glaucma occurs when pressure builds up in the eye. The pressure causes drainage of the aqueous humour to slow down in most cases, so that it builds up in the anterior chamber. The pressure pinches the blood vessels which carry blood to the retina and optic nerve. Vision is gradually lost because the retina and nerves become damaged.4

Many people without diabetes get cataracts, but people with diabetes are 60% more likely to develop this eye condition. People with diabetes also tend to get cataracts at a younger age, and they progress faster. The eye's clear lens clouds with cataracts, blocking light.4

**Foot complications**

People with diabetes develop various foot problems.1 Nerve damage leads to tingling, burning and weakness in the foot.5 It also lessens the ability to feel pain, heat and cold.4 A foot injury goes unnoticed until the skin breaks down and becomes infected. Nerve damage also leads to changes in the shape of the feet and toes. Diabetes causes changes in the skin of the foot. The foot becomes very dry at times. The skin peels and cracks. The problem is that the nerves which control the oil and moisture in the foot no longer work. Calluses occur more often and build up faster on the feet of people with diabetes. This is because there are high-pressure areas under the foot. Calluses, if not trimmed, become very thick, break down and turn into ulcers (open sores). Ulcers occur most often on the ball of the foot, or on the underside of the big toe. Ulcers on the sides of the foot are usually due to poorly fitting shoes. Neglecting ulcers results in infections, which, in turn, can eventually lead to the loss of a limb.5

Loss of feeling is particularly important because it allows injuries to go unnoticed, leading to serious infections and possible amputations. People with diabetes carry a risk of amputation that is more than 25 times greater than that of people without it.

**Skin complications**

Skin complications include bacterial infections, fungal infections and itching. Other skin problems occur mostly or only in people with diabetes. These include diabetic dermopathy, diabetic blisters, necrobiosis lipoidica diabeticorum and eruptive xanthomatosis.5

**Pregnancy complications**

Women with any type of diabetes during pregnancy risk having a number of complications if they don't carefully monitor and
manage their condition. Women with type 1 or type 2 diabetes should achieve target glucose levels before conception to prevent possible organ damage to the foetus. Women with type 1, type 2 or gestational diabetes during pregnancy should strive for the target blood glucose level throughout pregnancy to minimise complications. High blood glucose during pregnancy leads to the foetus gaining excess weight. This creates problems with the delivery, and results in trauma to the infant and mother and a sudden drop in blood glucose for the infant after birth. Children who are exposed for a long time to high blood glucose in the womb are at higher risk of developing diabetes in the future.5

**Oral manifestations and complications**

Xerostomia (a dry mouth), is brought on by diabetes and its symptoms in particular.1 A dry mouth leads to soreness, infections, ulcers and tooth decay. Diabetes also causes inflammation in the gums and thrush of the mouth and tongue.10

The body parts that are affected by diabetes and the resulting health-related problems are listed in Table I.

**Measures to prevent diabetes complications**

By keeping the blood glucose level in a healthy range through meal planning, physical activity, taking prescribed medications and implementing lifestyle changes, the long-term complications of diabetes may be avoided or lessened (Tables II and III).7

**Conclusion**

Diabetes is a chronic, manageable condition for which major changes in lifestyle are required to optimise its management. The pharmacist plays an important role by educating high-risk changes in lifestyle are required to optimise its management.

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<th>Table I: Body parts affected by diabetes and the resulting health-related problems</th>
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| **Blood vessels and heart** | • High blood pressure  
• Heart disease  
• Heart attack  
• Poor blood circulation or flow throughout the body  
• A stroke |
| **Nerves** | • Problems with the digestion, bladder, sexual dysfunction, and keeping the heart beat and blood pressure steady  
• Pain, tingling, numbness or weakness in the hands, arms, legs or feet |
| **Kidneys** | • The build up of waste and fluid in the blood  
• Protein loss through the urine |
| **Mouth** | • A dry mouth  
• Gum disease and loss of teeth  
• Thrush |
| **Eyes** | • Loss of vision and blindness  
• Cataracts |
| **Feet** | • Sores  
• Infections  
• Amputation |

**Table II: Measures to prevent diabetes complications**

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| **Healthy eating** | Follow a healthy eating plan and make wise food choices to lose weight, if needed, and to improve well-being  
Learn what to eat to keep the blood glucose level under control |
| **Self-monitoring of blood glucose** | Check and record the blood glucose every day  
Treat low blood glucose quickly |
| **Physical activity** | Moderate to high levels of physical activity and cardiorespiratory fitness are associated with a substantial reduction in morbidity and mortality in both type 1 and type 2 diabetes mellitus  
People with type 2 diabetes derive the following benefits from regular physical activity:  
• Increased cardiorespiratory fitness  
• Improved glycaemic control  
• Decreased insulin resistance  
• An improved blood lipid profile  
• Improved blood pressure  
• The maintenance of weight loss  
• Reduced abdominal and overall fat percentage  
• Improved well-being  
• Decreased stress and anxiety |
| **Medicines** | Take as prescribed by the doctor |
| **Cardiovascular** | A number of measures are important to reduce the risk of cardiovascular (heart and blood vessel) disease:  
• A blood pressure reading below 140/90 mmHg, and perhaps below 130/80 mmHg, is recommended for most people with diabetes who do not have kidney complications. A lower blood pressure goal (less than 130/80 mmHg) is recommended for people with diabetes who also have kidney disease  
• Manage high blood pressure with lifestyle modifications and/or medication  
• Quit smoking  
• Have a blood test to measure cholesterol and triglyceride levels, and modify the diet if needed. Some people will also need treatment to lower low-density lipoprotein (“bad cholesterol”) or triglycerides  
• Aspirin (81-100 mg per day) is recommended for anyone with diabetes who already has or is at increased risk of cardiovascular disease |
| **Kidney** | A urine test which measures the amount of protein (albumin) in the urine determines if diabetes is affecting the kidney's filtering action. Microscopic amounts of albumin in the urine (microalbuminuria) are an early indicator of diabetes-related kidney complications. The amount of albumin in the urine also helps to determine if the nephropathy is worsening  
An angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker is generally recommended if the albuminuria does not improve, even if the blood pressure is normal. People with an elevated blood pressure and albuminuria are also treated with an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker. These medications decrease the amount of protein in the urine and prevent or slow the progression of diabetes-related kidney disease |
| **Ketoadisis and ketones** | Ketones are detected with a simple urine test, using a test strip, similar to a blood-testing strip |
Many experts advise to check the urine for ketones when the blood glucose is more than 240 mg/dl (13.3 mmol/l)

Eye
Regular eye examinations are essential for detecting eye complications at an early stage, when the condition can be monitored and treated to preserve vision

Feet
Self-examination
A self-examination includes the following:
• Avoid going barefoot, even at home
• People with diabetes should examine their feet every day. It is important to examine all parts of the feet, especially the area between the toes. Look for broken skin, cuts, ulcers, blisters, areas of increased warmth or redness, sores, swelling, or sore toenails or changes in callus formation
• Wash the feet daily
• Test the water temperature before stepping into a bath
• After bathing, dry the feet and seal in the remaining moisture with a thin coat of plain petroleum jelly, an unscented hand cream, or other such products
• The extra moisture may lead to infection
• Too much callus formation may mean that therapeutic shoes and inserts will be needed
• Using a pumice stone every day will help keep the calluses under control. It is best to use the pumice stone on wet skin. Apply lotion after using the pumice stone
• Socks should fit and be changed daily
• Trim toenails to the shape of the toe
• Remove sharp edges with a nail file. Do not cut the cuticles
• Shoes should be snug, but not tight, and customised if the feet are misshapen or have ulcers

Clinical examination
During a foot examination, the doctor will look for changes such as ulcers, cold feet, thin skin, a bluish skin colour and skin breaks associated with athlete’s foot. The doctor will also test the sensation in the feet to determine if it is normal or diminished. People with decreased sensation are at risk of foot injuries which go unnoticed because of lack of pain

Pregnancy
The control of diabetes and its potential complications is especially important in women who are planning to become pregnant, as well as in those who already are pregnant. Controlling blood sugar levels before and during pregnancy decreases the risk of many complications in both the mother and infant

Mouth
To prevent and treat a dry mouth:
• Keep the blood sugar within the recommended range
• Clean the teeth after each meal and before bedtime
• Brush braces or dentures after each meal, if relevant
• Keep hydrated by drinking water
• Use a non-alcoholic mouthwash
• The use of lip balm is recommended for dry or irritated lips, particularly at the corners
• Floss at least once a day

Together with regular examinations for microvascular and macrovascular complications, with appropriate and timely interventions, is important to prevent or reduce morbidity and mortality.

References

Immunisation
High blood sugar weakens the immune system.
Recommendations are to:
• Have an influenza vaccine every year
• The doctor is likely to recommend the pneumonia vaccine, if indicated
• The Centers for Disease Control and Prevention also recommends a hepatitis B vaccination if not previously vaccinated against hepatitis B. It advises that vaccination occur as soon as possible after diagnosis with type 1 or type 2 diabetes

Smoking
Smoking increases the risk of various diabetes complications, so it is important to quit

Alcohol
Alcohol, as well as drink mixers, cause either high or low blood sugar, depending on how much alcohol is consumed and if food is eaten at the same time. If alcohol is consumed, do so in moderation and always with a meal.

Table III: Targets for haemoglobin A1c, fasting plasma glucose and postprandial glucose in different patient types

Patient type | Target HbA1c | Target FPG | Target PPG
--- | --- | --- | ---
Young | < 6.5% | 4.0-7.0 mmol/l | 4.4-7.8 mmol/l
Low risk | | | |
Newly diagnosed | | | |
No cardiovascular disease | < 6.5% | | |
Majority of patients | < 7% | 4.0-7.0 mmol/l | 5.0-10.0 mmol/l
Elderly | | | |
High risk | | | |
Hypoglycaemic unaware | | | |
Poor short-term prognosis | < 7.5% | 4.0-7.0 mmol/l | < 12.0 mmol/l

FPG: fasting plasma glucose, HbA1c: haemoglobin A1c; PPG: postprandial glucose


