25. Diabetes mellitus – type 1 diabetes

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Summary

Type 1 diabetes is a chronic disease with hyperglycemia (elevated or abnormally high blood sugar levels) due to insulin deficiency. Type 1 diabetes is treated with insulin, often with multiple injections daily.

In patients with type 1 diabetes, blood glucose levels change during physical activity, to a large extent because of insulin levels in the blood. Because insulin levels during exercise are most often higher in diabetics than in non-diabetic individuals, an effect of the treatment, hypoglycemia can easily arise during exercise. The tendency to hypoglycemia can persist for many hours after an exercise session. However, this risk can be avoided by planning diet and insulin doses in connection with physical exercise, and can likely also be reduced through physical training.

Regular physical activity increases the sensitivity to insulin, primarily in the skeletal muscle, which leads to a reduced need for insulin. Because diabetes is associated with a substantially increased risk for developing cardiovascular disease, physical training is very important for this patient group, as with non-diabetics, to influence risk factors such as elevated blood lipid levels and high blood pressure. Control of blood sugar, measured as glucosylated haemoglobin (HbA1c), has not shown to be significantly affected by physical training in the studies reported in the literature. It cannot be ruled out, however, that one may be able to achieve improved glucose control in individual cases by combining physical activity with other measures.

As is true for most people, patients with type 1 diabetes should engage in physical activity for a minimum of 30 minutes per day, at an intensity of at least moderate level, such as a brisk walk, cycling, etc. To attain further health and aerobic fitness effects, this

should be combined with physical activity/exercise/training of somewhat higher intensity at least 3 times per week, for example, a fitness class, ball sports, skiing, or similar activity depending on the person's interests.

Definition

Type 1 diabetes is a chronic disease that involves hyperglycemia (increased or abnormally high blood sugar levels) due to insulin deficiency. The disease was earlier called childhood- or juvenile- or insulin-dependent diabetes, but these descriptions should no longer be used.

Prevalence/Incidence

The onset of type 1 diabetes can be at any age, but is most common in children and young adults, with an increased risk during the preschool years and during puberty. The disease is found in most countries, but the annual incidence varies widely: in Europe, between 3/100,000 in the Balkan states to 30–40/100,000 in Scandinavia and Sardinia. In Sweden and Norway, it is estimated that 4/1000 develop type 1 diabetes before the age of 15 years, and a total of 7/1000 before the age of 35 years. Type 1 diabetes has long been considered responsible for 10–15 per cent of all diabetes, but it is possible that this number is larger in reality due to overlooked autoimmune diabetes that develops in the elderly.

Cause

In most cases (> 90%), the disease is caused by an autoimmune process that gradually destroys the insulin-producing beta cells in the islets of Langerhans. The exact cause of the disease has not been established but appears to be complex. Surrounding factors likely trigger type 1 diabetes in individuals with a genetic predisposition. Twin studies have shown concordance for the disease in 30–50 per cent of monozygote (identical) and 5–15 per cent in dizygote (fraternal) twins. Several genes are believed to be responsible for the inherited background, with the strongest link found in genes that code for HLA (DR-3 and DR-4) in the major histocompatibility complex (MHC) region on chromosome 6. There is also an increased co-occurrence of type 1 diabetes and other autoimmune diseases such as struma lymphomatosa (Hashimoto's thyroiditis), pernicious anaemia and Addison's disease.

Risk factors

Among the external factors that could initiate the autoimmune process in endocrine pancreas, discussion has concentrated on primarily viral infections. An increased development of type 1 diabetes during the fall and winter could be related to viral epidemics, but also to the cold (which can lead to decreased glucose tolerance and increased need for

insulin). Other risk factors that have been put forward, though not indisputably proven to play a role, are nitrosamines in food and early exposure to the protein in cow's milk. And finally, it is likely that the autoimmune process in the pancreas can accelerate in individuals who are growing rapidly (as in puberty), in infections, and in connection with stressful events.

Pathophysiological mechanisms

Even before the onset of clinical diabetes in the islets of Langerhans, signs of chronic inflammation can be seen, so-called insulitis, with infiltration of macrophages, T- and B-lymphocytes, and ongoing destruction of beta cells. In most patients with established type 1 diabetes, the beta cells have completely disappeared. At the clinical onset, patients have elevated titres of autoantibodies to glutamic acid decarboxylase (GAD) in almost 80 per cent, and tyrosine-phosphatase IA-2 in over 55 per cent of cases. Over 90 per cent have a positive titre if GAD and IA-2 are combined. Insulin antibodies have also been shown. Studies have shown that elevated antibody titres are present before onset of the clinical symptoms. It is unclear, however, whether these antibodies play an active role in beta cell destruction or rather appear secondary to this.

Symptoms and prognosis

Untreated type 1 diabetes leads to severe insulin deficiency with hyperglycemia and ketoacidosis. Symptoms of this condition include abnormally high secretion of urine (polyuria), excessive thirst (polydipsia), emaciation and fatigue. Despite as optimal insulin treatment as possible, there is a risk for developing both acute complications in the form of hypo- and hyperglycemia, and late complications related to the eyes, nervous system, kidneys and cardiovascular system. These complications can have an impact on the patient's ability to engage in physical activity.

Diagnostics

Diabetes is defined as a fasting plasma glucose of 7.0 mmol/l or higher, symptoms of diabetes and random plasma glucose measurements of over 11.0 mmol/l, of plasma glucose over 11.0 mmol/l two hours after intake of 75 g glucose (oral glucose tolerance test). At onset of type 1 diabetes, plasma glucose levels are typically over 20 mmol/l, most often accompanied by an increased ketone body production and sometimes acidosis. C-peptide levels in the blood can be low and as a rule the patient has positive titres for GAD and IA-2 antibodies.

Treatment

The treatment for type 1 diabetes is insulin. This often occurs in multiple injections daily, for example, with rapid-acting insulin before meals and medium-acting insulin at night,

or a mixed insulin (rapid and intermediate-acting) before breakfast and the evening meal. Insulin can also be administered via an insulin pump.

Effects of physical activity

Effect of acute exercise

In patients with type 1 diabetes, blood glucose levels change during physical activity, to a large extent because of insulin levels in the blood. It is thus important to consider the type of insulin (rapid- or long-acting) that the patient takes and the time interval between insulin injection and activity. Blood glucose levels fall in hyperinsulinemia during the physical activity if the latter is long-lasting (more than 30–60 minutes) or intensive, if more than three hours has passed since the last meal, and if the patient does not eat more before and during the activity (1, 2). Blood glucose levels can be lower than normal for up to 24 hours after an exercise session. On the other hand, blood glucose levels can rise in hypoinsulinemia, during vigourous exercise, or with the intake of large amounts of carbo-hydrates before and during the activity.

Effect of regular exercise training

Physical activity increases the sensitivity to insulin, primarily in the skeletal muscles, which leads to a reduced need for insulin (2–4). Control of blood sugar, measured as glyc-osylated haemoglobin (HbA1c), has not shown to be significantly affected by physical training in the studies reported in the literature (2, 4). It should, however, be noted that these results come from groups of study subjects that performed standardised training programmes and it cannot be ruled out that, some individuals may be able to achieved improved glucose control by combining physical activity with other measures. Because diabetes is associated with a substantially increased risk for developing cardiovascular disease, it is also important that physical training in this patient group leads to a reduction of the risk factors for heart disease, for example, improved blood lipid profile and lower blood pressure (4–6). Otherwise, in type 1 diabetes, the body appears to adapt to exercise training with normal increases of maximal oxygen uptake and of the muscles' capacity to burn energy (mitochondrial oxidative capacity), while the increase in the degree of capil-larisation of muscles with training can be somewhat decreased in type 1 diabetes (8, 9). The increased oxidative capacity in a given exercise leads to a larger part of the energy requirements of the musculature being met by burning fat. This should mean that the risk for hypoglycemia is reduced, at least during moderately intensive exertion, in physically fit persons with type 1 diabetes, but the research data in this area is still insufficient (10).

Indications

Primary prevention

There is nothing to suggest that physical activity can prevent the development of type 1 diabetes.

Secondary prevention

Regular physical activity is recommended for people with type 1 diabetes, but special care must be taken to avoid hypoglycemia (1). It is not certain that physical activity leads to better control of blood glucose, but there is nevertheless improvement in blood lipids and other risk factors for cardiovascular disease (4–6). No studies at present suggest that physical activity prevents diabetes' late complications. It cannot be ruled out, however, that one may be able to achieve this goal on an individual basis via improved glucose control through a combination of physical activity and other measures.

Prescription

As is true for most people, patients with type 1 diabetes should engage in a minimum of 30 minutes of physical activity per day, at an intensity of at least moderate level, such as a brisk walk, cycling, etc. To attain further health and aerobic fitness effects, this should be combined with physical activity/exercise/training of a somewhat higher intensity at least 2–3 times per week, for example, a fitness class, ball sports, skiing, or similar activity depending on the person's interests (see also Table 1). Strength training is also recommended (Table 1). If cardiovascular symptoms exist, the strength training should be less strenuos than shown in the table, for example 12–15 repetitions instead of recommended 8–12. In the case of eye symptoms, even lighter weights should be used and 15–20 repetitions of each exercise be performed. In order to avoid a rise in blood pressure, lifts should be done on exhalation and the muscles relaxed during inhalation. For aerobic fitness and strength training, each session should begin with a warm-up and end with a cool-down period of 5–10 minutes each, including careful stretching of tight muscles and soft tissues.

The physical activity should be planned carefully, with measurement of blood glucose before and after (and sometimes during) the activity session. A suitable blood glucose interval before exercising is 6–15 mmol/l. If the blood glucose level is over 15 mmol/l and/or ketosis occurs, the person should not exercise, and if the blood glucose level is under 6 mmol/l, he or she should definitely eat more before exercising. If possible, schedule the physical activity one to two hours after a meal, and more than one hour after insulin injection. Avoid injecting insulin in parts of the body that are active during the exercise. If necessary, reduce the preceding dose of insulin by 30–50 per cent, especially before extensive training or in the case of regular exercising. Even the dose of insulin after the physical activity may need to be reduced (5).

Take along some "fast carbohydrates" in the form of dextrose tablets, energy drinks or fruit during the training. During long exercise sessions, it can be necessary to take 15–30 g dextrose every 30 minutes.

Table 1. General recommendations for physical activity in diabetes mellitus – type 1 diabetes (11).

Type of training	Examples of activities	Frequency	Intensity	Duration
Basic activity	Walking, climbing stairs, gardening. It is also desirable to increase standing/walking time at work and in the home.	Daily	So talking is still possible, 30–50% of maximal oxygen uptake; 12–13 acc. to Borg's scale	> 30 min.
Aerobic fitness training	Nordic walking, jogging, cycling, swimming, skiing, skating, fitness class/aerobics/dance, ball sports, rowing	3–5 days/week	Until out of breath Begin slowly and gradually increase to 40–70% of maximal oxygen uptake; 13–16 acc. to Borg's scale*	20–60 min.
Strength training	Movements using the body as resistance, resistance bands, weights, weight/resistance equipment	2–3 days/week	Until or near muscular exhaustion for each exercise**	8–10 exercises, with 8–12 reps of each exercise

* Level of exertion may need to be reduced in the case of retinal, renal or cardiovascular complications as well as autonomic dysfunction.

** Replace with easier exercises in the case of retinal, renal or cardiovascular complications.

Functional mechanisms

Blood sugar concentration is a result of the balance between the liver's ability to release glucose into the blood stream and the uptake of glucose by the tissues. At rest, the liver releases approximately 7.5 g sugar per hour, most of which (about 6 g/hour) is consumed by the central nervous system and the tissues that lack the capacity of aerobic metabolism, above all the red blood cells. During physical exercise, the picture changes in that the working muscles' glucose uptake increases dramatically. For example, a person burns about 30 g of carbohydrates per hour of walking, whereof 15–20 g is covered by blood sugar. In moderate running, carbohydrate utilisation can increase to 90–100 g per hour, whereof about a quarter is covered by blood sugar (7).

The normally precisely regulated balance between glucose released by the liver and taken up by the tissues is easily disrupted in connection with exercise in people with type 1 diabetes. Normally, physical exertion leads to a sharp drop in the concentration of insulin in the blood. This is a result of the powerful activation of the sympathetic nervous system that occurs in connection with physical exertion, which leads to impairment of the insulin-producing cells. The fact that the sugar uptake of the muscles increases sharply in connection with exertion, despite the low insulin level in the blood is due to a non-insulin-dependent increase in the permeability of sugar to the muscle cells. In type 1 diabetes, this delicate

regulation can be disrupted by the insulin left in the blood from the previous dose of insulin, which tends to both increase the skeletal muscle's glucose uptake and decrease the glucose released by the liver (2). The result is that hypoglycemia easily arises during exertion, and can persist for many hours after an exercise session (1). The skeletal muscle's increased sensitivity to insulin that is present for 1–2 days after an exercise session, largely caused by a drop in muscle glycogen levels also contributes to the persistence of the hypoglycemia (2, 3). Exercising leads to a significant increase in the muscles' metabolic capacity (mito-chrondrial oxidative capacity) (8). In a given exercise, this leads to a larger part of the energy requirements of the muscle being met by burning fat. The reduced use of carbohy-drates during exertion can be considerable and can lower the needs of the musculature for blood sugar during exertion by 20 per cent or more, thereby reducing the risk for exercise-induced hypoglycemia.

In poor diabetes regulation with high blood sugar and a tendency to ketosis, an exercise session can yield the opposite effect, that is, hyperglycemia. The reason for this is unclear, but likely has to do with insulin deficiency that produces high blood sugar, at the same time as the increase in the skeletal muscle's sensitivity to insulin, as a result the exercise, can be reduced, for example, as a result of high levels of fatty acids and ketone bodies in the blood (2).

Functional tests/Need for health check-ups

In some cases, especially in older patients or in the case of long diabetes duration, it is appropriate to conduct a stress test or other examination to assess heart status. The presence of peripheral and autonomic neuropathy, impaired sensation, impaired joint function and proliferative retinopathy should also be assessed, as should kidney disease. The latter are necessary because elevated blood pressure during activity may aggravate eye problems and the development of kidney disease. And finally, one should examine the feet with respect to loss of sensation, uneven loading, pressure sores and hyperkeratoses, as well as the presence of sores.

Interactions with drug therapy

Physical activity increases both insulin sensitivity and insulin-independent glucose uptake in muscle, and thus enhances the insulin effect.

Contraindications

Absolute

- Hyperglycemia and/or ketosis.

Relative

- Caution with concurrent heart disease.
- In the case of peripheral neuropathy, there is a risk for injuries to the feet and joints.
- In the case of proliferative retinopathy, there is a risk for exacerbation of eye status (uncommon).
- In the case of autonomic neuropathy, physical activity that is too intensive can be associated with risks (hypotension and lack of early warning signs for cardiac ischaemia).
- In the case of kidney disease, high blood pressure (systolic pressure of 180–200 mmHg) can aggravate the development of the disease.

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