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Can Type 2 Diabetes Be Cured?

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ABSTRACT

Pathogenesis of Type 2 diabetes is complex and there is an interplay between genetic and environmental factors. While it is impossible to change genetic conditions at present, we do have an impact on the environmental ones. Symptoms of Type 2 diabetes usually increase slowly, and therefore the patient does not pay attention to them for a long time. If diabetes is diagnosed early, and treatment is carefully planned and carried out, it is possible in many cases to achieve recovery from the clinical symptoms. Nowadays we have many modern drugs available that greatly facilitate good metabolic alignment of Type 2 diabetes, but till 90s pharmacological treatment was limited to insulin, metformin and sulfonylurea. Treatment for Type 2 diabetes must be undertaken with a view to reducing insulin resistance. Studies show that proper diet and physical activity are much more effective in preventing the development of Type 2 diabetes than any drug available and they are both first treatment of choice. If this is not satisfactory, or if the patient is unsuccessful, pharmacotherapy is needed. Metformin is most often used at the beginning. If the treatment applied does not give satisfactory results, it is necessary to extend the pharmacotherapy – in this case, incretin drugs and Sodium-glucose linked transporter type 2 inhibitors (SGLT2 inhibitors) are recommended. Acarbose preparations (alpha-glucosidase inhibitors) are also used as supportive treatment. Currently, drugs from the sulfonylurea group are being introduced less and less often, as their use may cause hypoglycemic conditions as well as weight gain. When the use of oral medications appears to be insufficient for metabolic control, the inclusion of injections of insulin is considered.

INTRODUCTION

There is an interplay between genetic and environmental factors in the pathogenesis of Type 2 diabetes. While it is impossible to change genetic conditions at present, we do have an impact on the environmental ones. Insulin resistance is a very important factor leading to the clinical manifestation of diabetes [1,2], for which abdominal obesity is a very important determinant. We call this condition a metabolic syndrome [3,4,5,6]. Waist circumference (WC) measurement, waist/hip ratio (WHR) and waist/body height (WHtR – waist/height ratio) are used to assess abdominal obesity. According to the International Diabetes Federation 2005 criteria (IDF/2005 criteria), abdominal obesity in adults is diagnosed by adopting a waist circumference of 80 cm and 94 cm for women and men, respectively [7]. Excessive increase in fat cells during childhood can contribute to the development of obesity in adulthood. The increasing number of fat cells is unfortunately an irreversible process [8]. They accumulate not only in the subcutaneous and visceral tissues, but also in various organs, mainly in the liver, skeletal muscle, pancreas, blood vessels, heart, and kidneys. They change the cells' metabolism, and thus disrupt their proper functioning [9]. The adipose tissue is a very important secretory organ. In the development of insulin resistance, bioactive substances secreted are of substantial significance. They have endocrine, paracrine, and autocrine effects, causing tissue resistance to endogenous insulin. One of these substances is adiponectin, which has many functions in our body [10]. It plays an important role in maintaining insulin sensitivity of tissues, especially muscles, as well as of the liver and the adipose tissue itself. It activates fatty acid oxidation and increases insulin secretion. At the same time, apart from adiponectin, other substances are secreted by the adipose tissue, such as leptin, tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), resistin, and, above all, the product of lipolysis – free fatty acids (FFA), all of which are key to the development of insulin resistance [11]. Recently, a report on leptin-induced epigenetic modifications as well as epigenetic regulation of leptin in metabolic disorders has been published [12]. One of the important elements in the development of insulin resistance is the increased synthesis and release of proinflammatory cytokines, which also cause damage to pancreatic islet cells [13,14]. Decreased insulin sensitivity can be seen many years before Type 2 diabetes is diagnosed. Insulin resistance can lead to a number of disorders including the metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), and Type 2 diabetes [15,16,17]. Micro and macro-vascular complications are very aggravating complications of insulin resistance. Experimental studies have shown that fat storage in the heart can lead to cardiomyocyte necrosis, and affect myocardial contractility. A relationship

between insulin resistance and myocardial damage has been observed in clinical studies [18,19,20,21,22]. An increased influx of free fatty acids can also cause kidney damage [23], whereas the accumulation of fat in the liver cells can lead to chronic inflammation and fatty liver. The relationship between metabolic syndrome and periodontal changes has also been discussed in the literature – Gurav has introduced and elaborated on these issues extensively [24,25,26,27,28,29,30,31,32]. The author has noted the importance of early diagnosis of this complication. The LJM (limited joint mobility) syndrome may also be an early complication signaling the diagnosis of diabetes [33,34]. Diabetic patients often have accompanying endocrine disorders, including thyroid dysfunction [35]. Endocrinologist care is needed in such cases. Symptoms of Type 2 diabetes usually increase slowly, and therefore the patient does not pay attention to them for a long time. Unfortunately, the disease is usually diagnosed when chronic complications occur. This is already a period in which it is often impossible to reverse the symptoms of the disease. It is very important to systematically carry out glucose tolerance tests (OGTT) for people at high risk of the disease. The risk group includes people with obesity, hypertension, and heart disease, as well as with a family history of diabetes. It is worth mentioning that for early diagnosis of glucose tolerance disorders it is very useful to determine blood sugar levels in the glucose tolerance test also one hour after loading [36,37,38]. The basic principle of treating Type 2 diabetes is to change one's lifestyle, which means introducing a very well-defined, low-calorie diet, and maximally increasing one's physical activity, taking into account possible medical contraindications. Studies show that proper diet and physical activity are much more effective in preventing the development of Type 2 diabetes than any drug available. The diet should gradually reduce the number of calories consumed after about 500 kcal. A typical reduction diet, i.e. one that leads to a decrease in body weight, is 1000-1200 kcal/day. It is assumed that weight reduction should be at the level of 0.5-1 kg per week. If the patient does not lose weight, it means that the diet contains too many calories for the needs of their body. Of course, any diet that aims to reduce body weight should be supported by regular physical activity. If this is not satisfactory, or if the patient is unsuccessful, pharmacotherapy is needed. Metformin is most often used at the beginning. It is a drug that reduces insulin resistance. If the treatment applied does not give satisfactory results, it is necessary to extend the pharmacotherapy – in this case, incretin drugs and SGLT2 inhibitors are recommended [39,40,41,42,43,44,45]. The use of these drugs has been found to be beneficial in preventing diabetes complications [46,47,48]. Wilding et al. have proposed combining the SGLT2 inhibitor with an incretin drug as a beneficial solution in preventing cardiac complications [49]. Scheen has also presented the beneficial effects of combining a dipeptidyl peptidase-4 inhibitor

(DPP-4 inhibitor) with an SGLT2 inhibitor in the treatment of Type 2 diabetes [50]. American authors also presented a similar position [51]. Acarbose preparations (alpha-glucosidase inhibitors), which facilitate weight reduction, are also used as supportive treatment [52,53,54]. Currently, drugs from the sulfonylurea group are being introduced less and less often, as their use may cause hypoglycemic conditions as well as weight gain. When the use of oral medications appears to be insufficient for metabolic control, the inclusion of injections is considered. In this group of drugs, the decision to include insulin is usually the first priority. Of course, insulin is still a drug used in patients with Type 2 diabetes, but the indications for its use have changed. It should be remembered that in Type 2 diabetes, the secretion of endogenous insulin can be preserved for quite a long time, and it is often significantly increased in response to insulin resistance. The decision to start insulin therapy should be preceded by an assessment of insulin secretion. The simplest test is to determine the level of C-peptide [55,56]. Currently, more and more analog insulin preparations appear on the market, which may be useful in the treatment of Type 2 diabetes [57,58], however in obese patients insulin treatment should be seen as a last resort [59]. If we are dealing with very high hyperglycemia (≥ 300 mg/dl, i.e. ≥ 16 mmol/l) at the time diabetes is diagnosed with concomitant clinical symptoms, it is necessary to include insulin as soon as the diagnosis is made. Insulin therapy is often used transiently in these patients. This applies especially to the early periods of the disease when the function of β-cells is still preserved. Increasingly, when oral medications are ineffective, glucagon-like peptide-1 receptor agonist (GLP-1 RA) injections are used before insulin therapy [60]. Careful monitoring of early signs of chronic complications is also very important in patients. As part of such control, the level of glycated hemoglobin (HbA1c) and lipidogram should be tested periodically. Ophthalmologic monitoring is necessary as part of specialist consultations. It is assumed that every patient with diabetes requires ophthalmologic monitoring at least once a year. All patients over the age of 35 should also consult a cardiologist before commencing intensive physical exertion.

SUMMARY

The question posed in the title can be answered with "Yes" – diabetes can be cured as a clinically overt disease, provided that it is diagnosed at an early stage, that it is treated very vigorously, and, above all, that there is a definite reduction in obesity. However, one should keep in mind that genetic predispositions remain [61]. If the patient is diagnosed with Type 2 diabetes late when the complications are already developed and present, the patient requires a

very careful diagnosis and specialized treatment. In that case, we can no longer expect that the clinical symptoms will disappear; at most the treatment will slow down their development. That is why it is so important to diagnose metabolic syndrome and related diseases as early as possible.

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