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Diabetes in the context of dental treatment in an interdisciplinary approach

Julia Cabon¹, Julia Pejas¹, Anna Zawilska², Agata Trzcionka²

1 - Scientific Association at the Department of Conservative Dentistry and Endodontics of the Medical University of Katowice, Faculty of Medical Sciences in Zabrze,
Supervisor: dr Anna Zawilska, MD, PhD in Medicine

2 - Chair and Department of Conservative Dentistry with Endodontics, Medical University of Katowice, Faculty of Medical Sciences in Zabrze,
Head of Department: prof. dr hab. med. Marta Tanasiewicz, MD, PhD

Abstract

Introduction: Diabetes, including its numerous complications, is one of fundamental challenges of modern medicine. Over the years, many types of this disease have been appointed, differing in both etiological background and method of treatment.

Dentists, when providing dental care to a patient burdened with diabetes, should pay special attention to the first symptoms reported by the patient as well as manifested in the oral cavity and surrounding tissues, e.g. in the form of xerostomia, hypertrophy of the salivary glands, changes on mucous membranes, impeded healing, or difficulties in combating local inflammation and infections, as well as in the form of physiological microflora disorders.

Aim of the study: The aim of the study is to emphasize the need for controlling diabetes for the sake of general and oral health.

Materials and methods: Our work is mainly based on the articles published in PubMed, websites or medical books. We were looking for keywords such as 'diabetes', 'dental treatment', 'symptoms of diabetes' or 'oral cavity diseases'.

Results: Diabetes is often manifested by changes in the oral cavity, as evidenced by numerous scientific studies presented in the bibliography. Controlling the disease helps to eliminate lowering quality-of-life general symptoms and oral lesions.

Conclusions: Faced with the challenges of modern medicine, the dentist is obliged to inform the patient about the diagnostic and therapeutic possibilities of both diabetes itself and its symptoms occurring in the oral cavity and then take all steps to ensure that the patient's condition is stabilised.

Key words: diabetes; oral cavity diseases; diagnostics; dental treatment; symptoms of diabetes.

Introduction

Diabetes, as a representation of a group of metabolic diseases characterised by a concentration of serum glucose levels exceeding the norm, constitutes a major challenge in modern medicine. This is because it causes a number of complications, among which imbalances in carbohydrate, protein and lipid metabolism are notable. Equally significant are the possible distant complications arising from microangiopathic changes, such as retinopathy, nephropathy and diabetic neuropathy, as well as macroangiopathic changes associated with accelerated development of atherosclerosis and 'diabetic foot syndrome'. Their development depends on the degree of carbohydrate balance, the duration of diabetes and the existence of concomitant systemic diseases. In protecting patients from diabetes and its consequences, interdisciplinary cooperation and attention to symptoms signalling the onset and progression of this disease are particularly important.

1. Types of diabetes

Among the types of diabetes, we distinguish the following disorders of varying aetiology and aetiopathogenesis. The first type is type 1 diabetes mellitus (IDDM, insulin-dependent diabetes mellitus), in which there is destruction of the beta cells of the pancreatic islets, which occurs on an autoimmune basis following the action of triggering factors in predisposed individuals. The disease develops slowly, leading to a complete lack of insulin secretion and overt diabetes. Usually the first symptoms appear in children, adolescents and adults up to the age of 30, but cases of type 1 diabetes manifesting in patients aged 40-50 have also been reported. The disease is then referred to as LADA (latent autoimmune diabetes in adults), meaning autoimmune diabetes of late onset [3].

Another, and at the same time the most common type of diabetes, is considered to be a disease of civilisation - type 2 diabetes. It has been recognised by the United Nations as the cause of one of the major epidemics of the 21st century as the only non-communicable disease [2]. Studies point to the possible influence of genetic factors, but environmental factors are decisive in its development. The presence of abdominal obesity, excess body fat in non-obese individuals and low physical activity are particularly important.

The concept of 'lipotoxicity' manifested by inhibition of glycolysis in muscle and increased gluconeogenesis in the liver, reinforcing the need for compensatory overproduction of insulin, leading to depletion of tissue resources is also of relevance[3].

Another frequently diagnosed condition is gestational diabetes mellitus (GDM), which develops as a result of hormonal changes in the pregnant woman's body. Increased secretion of hormones with antagonistic effects towards insulin, results in the development of insulin resistance and consequently increased glucose accessibility to the foetus, with an imbalance in the carbohydrate metabolism of mother. Among the types of diabetes, there are also its types of unknown aetiology, such as drug-induced diabetes, diabetes in the course of genetic syndromes and genetic defects in the structure of the beta cells of the pancreatic islets and in insulin action.

2. Diagnosis of diabetes

Diagnosis for diabetes is based on the determination of the sugar concentration in the patient's venous blood. The person undergoing the test should be fasting, therefore the last meal should be consumed no later than 8-14 hours before the test.

Another type of test which can detect abnormalities of glucose metabolism is the oral glucose tolerance test (OGTT). This is a functional test that can detect both diabetes and its risk of abnormal glucose tolerance. The testing scheme is a two-stage procedure, namely fasting blood glucose is measured in the first stage and then 120 min after drinking a 75 g glucose solution. Each time, it is necessary to confirm whether the patient is following a diet with a normal carbohydrate content, as well as whether he or she is taking any medication that may increase glycaemia. Pharmacological agents with such effects include, among others, glucocorticosteroids, thiazide diuretics and some beta-blockers [10].

A further test applied in the diagnosis of diabetes is the determination of the glycated haemoglobin value (HbA1c), which assesses the patient's average glycaemia over the past three months. The determined HbA1c value is also a reliable indicator of the metabolic of diabetes control and, on its basis, the dentist can assess the degree to which the disease is controlled before proceeding with invasive procedures. According to the literature, two large clinical trials, namely the Diabetes Control and Complications Trial (DCCT) for IDDM diabetes and the United Kingdom Prospective Diabetes Study (UKPDS) for type 2 diabetes, have significantly reduced the risk of late-onset diabetes complications by setting guidelines for glycated haemoglobin limit values in individual clinical cases. A decrease in HbA1c value from 9 to 7 per

cent has reduced the risk of retinopathy by nearly 70 per cent, and neuropathy by 60 per cent and nephropathy by more than 50 per cent [9].

However, treatment of patients in these trials carried some risk of hypoglycaemic incidents and was associated with greater weight gain of a patient, and particularly intensive therapy (to achieve a glycated haemoglobin value below 6.5%) had some mortality rates, as confirmed by the prematurely discontinued 2007 'Action to Control Cardiovascular Risk in Diabetes' (ACCORD) study. [9].

Due to all medical reports, the value at which diabetes is considered to be regulated and well-controlled, the percentage of HbA1c $\leq 7\%$ is taken as the general criterion [5].

In the diagnosis of type 1 diabetes, the determination of anti-islet antibodies can be used to confirm or exclude an autoimmune aetiology of the disease. Autoimmunoglobulins determined in this manner include both typical anti-islet antibodies (ICA) and antibodies against the enzymes: glutamic acid decarboxylase and tyrosine phosphatase.

On the other hand, we use the determination of a marker of the degree of destruction of pancreatic islet beta cells in the form of C-peptide to determine the severity of the autoimmune process [10].

Another test to direct the diagnostic trajectory towards diabetes is the determination of ketone bodies in urine or the determination of their increased concentration in blood serum. In this test, strip tests are used, which are particularly sensitive to the presence of acetoacetic acid in body fluids.

So when do we diagnose diabetes?

Diabetes is diagnosed when:

- random blood glucose level ≥ 11.1 mmol/l (200 mg/dl) and typical symptoms of hyperglycaemia
- random blood glucose level ≥ 11.1 mmol/l (200 mg/dl) without typical symptoms of hyperglycaemia and on one occasion a fasting blood glucose ≥ 7.0 mmol/l (126 mg/dl)
- 2 times (determined on other days) fasting blood glucose ≥ 7.0 mmol/l (126 mg/dl)
- blood glucose at 120 min OGTT ≥ 11.1 mmol/l (200 mg/dl)

3. Symptoms of diabetes

Diabetes mellitus is characterised by a number of general symptoms which allow the initial diagnosis of the condition. These include: increased urination (polyuria), increased thirst (polydipsia), weakness, somnolence, susceptibility to purulent skin infections and genitourinary infections. One of the more serious symptoms can be - belonging to the emergency conditions- acidosis and ketone coma, which constitute acute complications of diabetes and can be life-threatening. Often, acidosis and ketone coma are the first symptoms of type 1 diabetes in young people [1,10].

The dentist should note, on the basis of the patient's history, the above-mentioned symptoms which the patient may be complaining about, and suggest a visit to the primary care physician's office to obtain a referral for appropriate tests. The dentist may also draw attention to the numerous changes which occur in the mouth in the course of diabetes and, on this basis, instruct the patient to undertake further diagnostics.

Numerous studies have shown that patients with poorly controlled diabetes have a significantly increased risk of developing any pathological changes in the oral cavity, therefore an early detection of the risk of disease or disease occurrence, and the initiation of treatment, improves the prognosis of the disease in terms of its course.

What changes in the oral cavity may suggest an initial diagnosis of diabetes and its development?

Clinical cases of chronic periodontitis are most commonly described in diabetics.

Chronic periodontitis (*periodontitis* in Latin) is a chronic infectious disease leading to the destruction of the tissues surrounding the tooth, i.e. the gingiva, the tooth suspension apparatus in the form of the periodontium, and the bone. According to sources, the development of *periodontitis* is influenced by both an immunological, genetic and infectious component (in the form of bacteria of the Socransky complex residing in periodontal pockets), as well as the degree of oral hygiene and a number of trophic changes caused by diabetes [12].

These include changes in the structure of peripheral vessels (angiopathic changes being a late complication of diabetes), or modifications to the gingival epithelial barrier, which affects the development of the inflammatory process in periodontal tissues and weakens their regenerative capacity due to reduced blood flow in the lumen of the altered vessels. In addition, intensive glycation processes accompanying hyperglycaemia in the course of diabetes alter the form of collagen, which is an important building block of periodontal structures, leading to its destruction.

Diabetic patients also often struggle with non-inflammatory and non-cancerous enlargement of

the salivary glands (*sialoadenosis* in Latin) and decreased secretion of saliva of altered composition, which may also imply other complications. Examples of these include oral thrush, altered mucosal morphology or high susceptibility of tooth tissue to caries [4,5,12].

Enlargement of the salivary glands occurs under the influence of intracellular inclusions in the form of lipid droplets, which are marked particularly in the acinar and ductal cells. Cytokeratins (CK), the basic elements of the cytoskeleton of epithelial cells, are then determined in preparations of tissue structures.

In addition, cytokeratins, released from intensely proliferating or apoptotic cells, are a tumour marker and, at the same time, an important indicator to assess the stage and progress of treatment of small-cell lung cancer and other epithelial cancers [7].

A 2004 study by Card et al. comparing the structure of the salivary glands of diabetics and patients with alcoholism showed that diabetics exhibited more intense cytokeratin marking at the cell limit level in the parotid gland acinar cells, even though some of the cells demonstrated overall greater reactivity than mononuclear salivary gland cells of a biopsy taken from a patient with alcoholism and a biopsy from a control sample [6].

Such immunohistochemical changes may suggest some modifications in the structure of the cytoskeleton of the acinar cell and in its degree of differentiation, as they do not normally express cytokeratin.

This study also confirmed that in the cellular structure of the salivary glands of diabetic patients, we observe an increased number and size of lipid droplets, which translates into an increase in the overall volume of the gland stroma and a widening of the ducts, while the size of the acini is reduced [6].

Another problem faced by diabetic patients is xerostomia and hyposalivation. The feeling of dry mouth resulting from a reduction in saliva secretion, especially unstimulated full saliva, is probably due to autonomic nerve dysfunction against a background of polyneuropathy or impaired microcirculation. This results in weaker stimulation reaching the salivary gland and the salivary gland itself becoming insensitive to stimuli that stimulate its secretory component to release saliva [4,5,8,12].

In diabetes, xerostomia may also result from dehydration of the patient associated with the phenomenon of osmotic diuresis, which develops due to inadequate control of blood sugar levels. It is also worth noting of a number of side effects which may be caused by drugs used in antidiabetic therapy. Numerous studies confirm that one of the drugs that can cause hyposalivation-induced xerostomia is metformin.

In the context of reduced salivary secretion, it is also important to bear in mind the aetiological factors of caries as an infectious disease caused by bacteria of the *Streptococcus* genus. The lack of a basic defence in the form of immune factors contained in saliva in the presence of inadequate oral hygiene, susceptibility of tooth tissues and a diet rich in sugars, results in a significantly increased risk of caries in diabetics. It is crucial to emphasise that the risk and prevalence of caries among diabetics varies significantly among different patient groups. Among type 1 diabetics, there is a reduced susceptibility to caries due to the fact that patients significantly reduce their sugar supply through a restrictive diet. However, the situation is different among patients with type 2 diabetes, where the risk of demineralisation and disintegration of tooth tissue is considerably higher.

A particularly notable oral condition often associated with diabetes is *Candida*-induced oral candidiasis, which implies other mucosal changes.

The reasons for the development of candidiasis in patients with poorly controlled diabetes are attributed to increased glucose concentrations in saliva and gingival fluid, as well as reduced production of antifungal immunoglobulins compared to healthy individuals or patients with well-controlled diabetes. Furthermore, due to the presence of a number of non-specific response factors in saliva in the form of histatins, or defensins, less saliva means a reduction in the quality of the local immune response to a potential *Candida albicans* infection [4,5,12]. In the case of pseudomembranous candidiasis in adults, it is worth immediately extending the diagnosis to diabetes mellitus and significant immunological deficiencies.

The symptoms that accompany yeast infection are most often the formation of white patches on the surface of the oral mucosa, which can be removed with cotton gauze, following which a reddened and bleeding area is exposed.

Another symptom of candidiasis is a burning sensation in the mouth, which should be differentiated with diabetic peripheral neuropathy, a late complication of the disease. The neurological origin of this symptom is supported by the accompanying burning sensory disturbance of taste (dysgenesis) and the dysfunction of other senses.

Oral mucosal diseases also encompass tongue lesions, which include fissured (furrowed) tongue,

atrophic glossitis, median rhomboid glossitis, and geographic tongue, or benign migratory tongue inflammation.

The first of these lesions, namely fissured tongue, is characterised by single or multiple furrows arranged parallel to the long axis of the tongue on its dorsal surface [11-14].

Atrophic tongue inflammation involving both the entire surface of the tongue and isolated areas is one of the lesions characteristic of, but not pathognomonic of, diabetes. Their occurrence has also been attributed to food deficiencies as well as other conditions independent of diabetes. However, studies have particularly pointed to the coexistence of lingual papillary atrophy with diabetes, and in particular with the often *Candida* yeast infection accompanying diabetes.

Focal atrophy of the lingual papillae is observed in conditions such as rhomboid glossitis, in which atrophy occurs among surrounding papillae arranged along a border line in the posterior part of the tongue, and benign migratory glossitis (geographic tongue), in which local atrophy of the papillae is observed, surrounded by raised and migrating edges [12-14].

Lichen planus or lichenoid lesions are significantly more frequently observed in the oral cavity in patients with diabetes mellitus.

According to the classification introduced by the World Health Organisation in 1978, there are several forms of lichen planus, namely vesicular, macular, erosive, atrophic and ulcerative forms [16]. It is also worth bearing in mind that the erosive form of lichen planus is a precancerous condition and if it occurs, the patient should be given special care and more frequent follow-up visits.

A study by Jaruchowska et al. conducted at the Department of Mucosal and Periodontal Diseases, IS WUM, revealed that among 31 subjects with lichen planus, 20% had co-existing type 2 diabetes mellitus, while among 153 patients with diabetes mellitus, six patients were diagnosed with lesions of the nature of lichen planus.[15].

4. Dental management of the diabetic patient

When considering the direction of the dental management of a patient with diabetes mellitus, it is necessary to consider the aspects mentioned above and the limitations related primarily to the impairment of the normal function of the immune system and, consequently, to the impediment of the tissue healing process and the fight against potential infections.

Long-term hyperglycaemia leads to an over-activation of the immune system in response to pathogens, therefore the over-produced inflammatory mediators closely associated with diabetes exacerbate tissue inflammation and reduce collagen synthesis, thus impairing intercellular matrix production and healing. These mediators include interleukin 1b, interleukin 6 and 8 and tumour necrosis factor TNF-alpha [17].

4.1 Patients of the Oral Surgery and Implantology Clinic - special recommendations

The patient presenting for a tooth extraction or other planned surgical procedure should receive special care to prevent local postoperative complications resulting from the burden of diabetes. Patients with uncontrolled or inadequately controlled forms of this disease are particularly at risk.

It is vital for the patient to have a tailored regimen for dental procedures with tissue disruption, but some standard regimens are known, depending on the type of disease.

Patients with type 1 diabetes, which is well controlled, should take half the daily dose of insulin in the morning after a meal, while after surgical intervention it is recommended that they take the full daily dose with the addition of rapid-acting insulin (e.g. Aspart Insulin).

Patients with type 2 diabetes should eat a meal and, depending on the treatment regimen, take the recommended dose of oral medication.

Before treatment, a diabetic patient's blood glucose level should be determined each time. If it is in the range of 100-200 mg/dl, the surgical procedure can proceed. If, on the other hand, it exceeds the limit of 200 mg/dl, the patient should be given intravenous dextrose solution and rapid-acting insulin introduced subcutaneously [5].

If there is a risk of hypoglycaemia (value < 70 mg/dl), then the procedure should be postponed, as this is a condition that can lead to unconsciousness and, consequently, coma and death of the patient. Early symptoms of hypoglycaemia include restlessness, sweating, pallor of the skin, increased blood pressure and pupil dilation, and when the critical period for the possibility of glucose administration is exceeded, central nervous system symptoms occur, manifested by disorientation, amnesia, confusion, convulsions and initially increased and then weakened tendon reflexes. In the end stage, coma is present.

The dentist should always be aware of the risk of acute complications of diabetes, including

specifically hypoglycaemia, therefore appropriate treatment should be implemented in the event of this condition. In mild hypoglycaemia, 10-20g of glucose should be administered, and in severe hypoglycaemia, 20% glucose solution should be given intravenously. Glucagon 1 mg by subcutaneous or intramuscular injection can also be substituted [20,21].

In the context of perioperative antibiotic therapy, it should be remembered that, according to the guidelines of the Polish Dental Society Force Task Group and the National Antibiotic Preservation Programme, only immunodeficient patients, which include those with uncompensated diabetes and poorly controlled glycaemia, may receive preoperative antibiotic prophylaxis in the form of a 'one-shot' administration 30-60 min before surgery.

The drug which is recommended if post-operative infection prevention is amoxicillin without clavulanic acid in a single dose of 2000 mg (for children 50 mg/kg b.w.), and in the case of allergy to penicillin group drugs, cefazolin 1000 mg (for children 50 mg/kg b.w.) or clindamycin 600 mg (for children 20 mg/kg b.w.) should be administered [19].

Considering the psychological aspect accompanying surgical procedures, the need for local anaesthesia should be taken into account. This is particularly relevant because catecholamines released in a stressful situation can cause an increase in heart rate and blood pressure and, importantly for diabetics, an increase in glucose levels.

Due to the inconsistencies surrounding the discussions on which drug should be applied in local anaesthesia in the diabetic patient, numerous studies have been conducted.

One significant voice was the 2015 study supervised by Marcel Alves dos Santos-Paul, which aimed to demonstrate that it is reasonable and safe to use vasoconstrictors in a topical analgesia preparation. In the example presented here, a small volume of vasoconstrictors was used in patients with type 2 diabetes mellitus and coronary artery disease, who constituted the study sample, in a 35 group, a small volume of anaesthesia (5.4 ml) containing 2% lidocaine with epinephrine at a concentration of 1:100 000 was administered, while in a second and equal-weighted group, only 2% lidocaine was used in the same volume [18].

Comparing the results, it was concluded that the use of an anaesthetic containing added epinephrine was safe and, interestingly, the data indicated that patients who received it had lower blood glucose levels.

Furthermore, the use of lidocaine analgesia with epinephrine was not shown to result in significant changes in haemodynamic parameters or patient anxiety levels, providing an additional argument for the use of a vasoconstrictor in local anaesthesia in patients with diabetes [18].

Although patients with well-controlled diabetes and proper glycaemic levels should be treated as potentially healthy patients, it is advisable not to make the false assumption that the patient is definitely in proper control of his or her disease. The doctor should always approach the patient's relationship with a certain degree of limited trust, and should therefore also control the glycaemia, and carry out the procedure itself in the least traumatic manner possible, dressing the postoperative wound appropriately and recommending proper hygiene, as well as informing about possible complications, especially in the case of patients with unbalanced diabetes.

4.2 Mucosal and Periodontal Disease Outpatients - special recommendations

Periodontal patients suffering from *periodontitis* or troublesome lesions occurring on the oral mucosa deserve special attention.

In the case of periodontitis, professional hygienisation can improve glycaemic parameters (especially the diabetes stabilisation index - glycated haemoglobin) and, consequently, the overall periodontal condition.

One study by Janket et al. revealed that in patients with type 1 and type 2 diabetes, average HbA1C values decreased by 0.38% after periodontal treatment, and in a group of patients with type 2 diabetes only, the decrease in glycated haemoglobin values was approximately 0.57% [23].

In the case of other problems, including suspected *Candida* yeast infection, appropriate diagnostics should be implemented in the form of a mycological examination with a possible antimycogram. As a result of the assessment of yeast sensitivity to drugs, appropriate therapeutic management should be initiated.

Initially, topical preparations should be used in the form of rinses, gels or suspensions with chlorhexidine, iodinated polyvinylpyrrolidone or nystatin (the addition of ice increases the activity of nystatin). It should be noted that nystatin and chlorhexidine therapy should not be used concurrently, as the biguanide derivative weakens the effect of nystatin. The literature also indicates the efficacy of topical clotrimazole and miconazole, which can also be used by intravenous injection or oral therapy [24].

Systemic antifungal therapy includes the use of fluconazole, or amphotericin B, and is given to patients unresponsive to topical therapy and to immunocompromised and severely affected patients [22].

In the case of pathological dryness of the mucous membranes, depending on its aetiology and the degree of preservation of salivary gland function, it is worthwhile to use pharmacotherapy to improve the patients' quality of life and their eating comfort.

In cases where salivary gland activity is partially preserved, drugs with a parasympathomimetic component, such as pilocarpine hydrochloride, which stimulates the receptors for salivary secretion, can be used. However, the use of this drug carries the risk of side effects such as persistent sweating, which can result in dehydration and electrolyte deficiencies. Other side effects may include frequent urinary urgency, reddening of the skin or excessive tearing. However, in order to reduce the potential risk of drug-induced myocardial conduction disorders, a thorough medical history should be taken and the patient's medication should be reviewed. Pilocarpine should be used with particular caution in patients taking beta-blockers [24].

When dryness significantly impairs the patient's quality of life, artificial saliva substitutes can also be used as an adjunct to therapy. Their action is based on the specificity of soluble polymers, particularly sodium carboxymethylcellulose and copolymers: polyoxypropylene glycol with polyoxyethylene glycols, which replace the action of native saliva [22].

For the treatment of lichen planus lesions accompanying diabetes mellitus, consideration should be given to current and past medical conditions, medications being taken and possible interactions between these and the planned therapy.

In the simple and uncomplicated form, herbal remedies and supplementation with vitamin A and B vitamins should be used, while in the more severe form, topical anti-inflammatory drugs, introduction of laser biostimulation and, in the case of multiple and extensive lesions, systemic corticosteroid therapy should be considered, bearing in mind all its limitations and possible side effects. The main limitation of topical corticosteroid therapy - apart from the side-effects of long-term therapy - is the great difficulty in applying and maintaining them on mucosal surfaces, and for this reason topical retinoids in paste form are seen as an alternative to steroids, due to their ability to remain longer on body surfaces.

In the available specialised medical literature, there is a statement that the most commonly used and effective treatment for symptomatic lichen planus (especially in the atrophic, ulcerative and erosive forms) is the topical agent of clobetasol propionate [25].

5. Conclusions

Diabetes, being a serious challenge for modern medicine, obliges dentists to a holistic approach to the patient and to face the local and systemic symptoms of this disease.

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