

Prophylaxis and prevention of vascular abnormalities in patients with diabetes mellitus

Diyabetes mellitus hastalarında vasküler anormalliklerin profilaksisi ve önlenmesi

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ABSTRACT

Diabetes mellitus is a hereditary metabolic disease which chronically progresses caused by absolute or relative deficiency of insulin hormone. In the course of time, diabetes mellitus causes damage to small, medium, and large blood vessels, as well as peripheral nerves. Herein, we review the prophylaxis and prevention of vascular abnormalities in patients with diabetes mellitus.

Keywords: Diabetes mellitus; prevention; prophylaxis; vascular abnormality.

Diabetes mellitus is a hereditary disease with chronically progressing metabolism caused by absolute or relative deficiency of a hormone called insulin.^[1] In the course of time, diabetes mellitus causes damage to small, medium and large blood vessels, as well as peripheral nerves. The high blood glucose level leads to development of early atherosclerosis.^[1] When the large and medium arteries are affected, macroangiopathy may present, of which clinical presentations are ischemic heart disease (myocardial infarction, stenocardia, etc.), chronic arterial limb insufficiency, and cerebrovascular disease. Microangiopathies are characterized by the extent of the damage to:

- Kidneys-diabetic nephropathy. Typical features include damage to glomerulus (glomerulosclerosis); arteriolosclerosis of

ÖZ

Diyabetes mellitus, insülin hormonunun mutlak veya göreceli eksikliğinden kaynaklanan, kronik olarak ilerleyen kalıtsal bir metabolizma hastalığıdır. Zaman içerisinde, diyabetes mellitus küçük, orta ve büyük kan damarlarında ve yanı sıra periferik sinirlerde hasara neden olur. Bu yazıda, diyabetes mellitus hastalarında vasküler anormalliklerin profilaksisi ve önlenmesi gözden geçirildi.

Anahtar sözcükler: Diyabetes mellitus; önleme; profilaksi; vasküler anormallik

nephritic vessels; interstitial nephritis, etc.^[2] An early symptom is microalbuminuria (albumin in urine 20-300 mg/24 hrs.). Kidney diseases are often accompanied by frequent urinogenital infections;^[2]

- Eyes-diabetic retinopathy. It is particularly typical for type 1 diabetes (it is developed in 90% of diabetes cases existing in excess of 10 years).^[3,4] It can be non-proliferative and proliferative. The latter is characterized by new growth of blood vessels in the retina. Typical features are also microaneurysms and hemorrhages. Central vision damage is likely to occur, as well as retinal exfoliation, and secondary glaucoma is likely to be developed;^[3,4]



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- Nervous system-diabetic neuropathy. Most often, it is of the peripheral sensory-motor polyneuropathy type. Its symptoms are sensory abnormalities and weakness phenomena, particularly in the limb area-tingling sensation (paraesthesia), impaired sensitivity to temperature, pain, contact, hyporeflexia, impaired vibration sensitivity (deep sensitivity).^[5] The autonomous (vegetative) nervous system is often affected as well-autonomous diabetic neuropathy. It is manifested by symptoms of various internal organs (they are being innervated by the vegetative nervous system)-heart abnormalities (most often rhythmic-conductive), gastrointestinal tract disorder (delayed stomach emptying, sense of swelling, difficulty in swallowing, alternating constipation and diarrhea, etc.), urogenital abnormalities, impaired thermoregulation, etc.^[6]

A special form of angiopathy is diabetic foot.^[7] It represents a combination of pathological changes in the lower limbs and feet caused by the developing vascular-degenerative syndrome and changes in the peripheral nervous system, which are common for patients who suffer from diabetes mellitus. Due to its utmost importance, it should be treated as a separate symptom complex-a special clinical unit, rather than as complications of different nature in diabetic patients only. Polyneuropathy results in the so-called neuropathic diabetic foot-marked by painless callous ulcers in the area of the heels and thumb-cushions, often caused by poor hygiene and injuries as a result of impaired sensitivity.^[8] If combined with macroangiopathy, the foot is cool, colored livid to copper red, with necrotic tissues on the thumbs and feet, and typical hobble is seen (claudicatio intermittens-periodical limp during walk). It is called mixed type or neuroischemic. Diabetic foot can be also purely ischemic. In roughly half the instances of patients with diabetic foot, diabetic polyneuropathy is leading, in 25% of the cases the ischemic component is seen only, while diabetic foot is of the mixed type in the remaining 25-30%.^[9]

During pathoanatomical examination, it is likely to detect diabetes-specific thickening of the basal membrane at the level of arterioles, pre-capillaries and capillaries, whereas in most cases complete vessel obliteration is not found.^[1,9] Apart from diabetic effects, macroangiopathy is associated with atherosclerosis: staged stenosis is available up to complete obliteration of the medium-sized peripheral vessels.^[1,9] Polyneuropathy is due mainly to endoneural vascular damage causing demyelination of the peripheral nerves, resulting in

poorly reduced sensitivity, particularly to temperature, pain, and contact.^[10]

A specific foot configuration is seen, while typical deformations and hyperkeratosis (callus) are found as a result of the growing plantar atypical loads.^[7,9] Fissures are often seen near the calluses and atypical deformations. Microtraumas, fungal infections of the toes and various minor injuries due to wearing uncomfortable shoes are of common occurrence.^[7,9] All of them, in return, serve as the gateway to largely trivial infections, which in combination with poorly treated diabetes may lead to foot phlegmon and gangrene.^[7,9,10] A typical feature of the neuropathic diabetic foot is the characteristic ulcer in the points of highest load, surrounded by hyperkeratosis, which is infected in most of the cases.^[11] Depending on the ulcer depth, four clinical stages are differentiated:^[11]

1. Superficial ulcer.
2. Ulcus reaching the joint capsule and/or tendon.
3. Ulcus with evidence of abscess, purulent arthrosis, osteomyelitis.
4. Foot necrosis and gangrene.

For clinical practice and treatment choice, it is of utmost importance to distinguish between neuropathic and ischemic ulcer.^[12] Typical features of neuropathic ulcer are absence of pain, poorly impaired sensitivity, warm and even inflamed foot; foot pulsations are seen as a rule, localization is over the plantar surface, hyperkeratosis around the ulcer is typical and forms a corn/callus. In the case of ischemic ulcer, not only diabetes, but also hypercholesterolemia and arterial hypertension are found.^[11,12] The patients are often chronic smokers.^[11,12] The ulcer is localized mainly on the fingertips or heel, and it is painful and highly sensitive at a touch. Shortened claudicatio intermittens is present, as well as foot pulsation is weakened; callus is not found; the bottom is necrotic with partial granulations.^[13]

In our study conducted two years ago with 159 patients including 114 men and 45 women who were treated at the Vascular Surgery Department at MBAL - Burgas AD for various diabetic foot complications, we found that 117 of them searched medical advice too late - 10 and more days after the disease onset.^[14,15] This can be explained by the unawareness of patients, tendency to self-treatment, and treatment by persons without required qualifications to treat seemingly small sores on the feet. The treatment of diabetic foot with an infected wound is, therefore, fatally delayed

and the consequences are most often irreversible followed by a high limb amputation.^[15,16]

The treatment of diabetic foot is an extremely challenging with slow progression.^[16,17] For diabetic foots, vascular surgical revascularizations are performed with the same goal to eliminate the ischemic component of the disease. These revascularization procedures include thromboendarterectomy, and femoropopliteal or femorodistal bypasses.^[15] Modern methods in this direction involve the so-called hybrid operations, including not only the aforementioned methods, but also balloon dilatation and stenting on the distal segments of the shank arteries.^[9,15]

On the other hand, the approach to the infected neuropathic ulcer is different.^[18] In such cases, local treatment is critical. The requirements include bed rest, foot load relief using special orthopedic footwears, and surgical treatment of calluses/resection/treatment with various disinfectants and curative unguents/dermazin, jodasept, 5% salicylic ointment. In the case of phlegmon, purulent arthritis and osteomyelitis, wide incisions and counter incisions are performed, as well as the excision of necrotic tissues and tendons, removal of osteomyelitis- affected bones, and drains. Samples for microbiological analysis are collected. In those cases, it is required to apply wide-spectrum antibiotics in combination with metronidazole, while diabetes correction is compulsory. Provided a pressure chamber is available, it is recommended to carry out oxygen therapy, particularly, when anaerobic infection is present.^[19] A simpler method involves putting the limb in an oxygen tent.^[19] Recently, the method of permanent aspiration in exudation wounds also attracts a growing number of followers. A special bandage is made and placed at a vacuum of 0.1-0.2 atm.^[19] The results of the treatment in our department are given in Table 1.

Briefly, different-size surgical approaches were required to be performed in all patients, where 84 of them had vascular reconstruction initially for limb revascularization. Nevertheless, the share of high amputations /shank and thigh/ was significant-52 or 33.12% of all patients. Moreover, it is impressive to observe that high amputation was required on seven patients only from those having reconstruction, while

the rest underwent smaller interventions. This allows to draw a conclusion that vascular reconstruction should not be abandoned even in aggravated cases of neuroischemic diabetic foot.

At present, the occurrence of type 1 diabetes cannot be prevented (preventive measures of proven efficiency not identified).^[20] Environmental factors, yet not completely specified, unlock an immune system reaction which gradually destroys your own insulin-producing cells within the pancreas (autoimmune disease). Type 1 diabetes usually occurs suddenly and dramatically (in view of the absolute insulin deficiency leading to metabolic acidosis), while type 2 diabetes symptoms often can be mild or completely missing, which makes difficult to diagnose this type of diabetes at its onset.

As people suffering from type 1 diabetes lack their own insulin production, this hormone will be added exogenously. About 5 to 10% of all diabetic patients suffer from this type of disease.^[21] However, type 2 diabetes can be prevented in many cases by achieving a healthy body weight and doing moderate, but regular physical exercises. This fact has been also confirmed by several clinical studies conducted in China, Finland, and USA.^[21] Unless primary prevention measures for type 2 diabetes are taken immediately, health systems would not be able to cope with the epidemic of diabetes in the near future, in particular, considering the ageing of population and an increased number of individuals at the retirement age. Therefore, it is essential to invest in programs of primary prevention (prophylaxis) of type 2 diabetes by increasing public awareness on the disease prevention and also of early identification of high-risk individuals. This may also help to save financial resources in the future thanks to suspension or delay in the development of type 2 diabetes and its associated complications, such as diabetic foot.

The International Diabetes Federation published a type 2 diabetes prevention consensus in 2007 suggesting three simple steps:^[17]

1. All individuals at risk to develop type 2 diabetes should be actively identified by completing a simple questionnaire for evaluation of risk factors, such

Table 1. The results of treatment in our department

| Operation | Incision excision necrotomy | Amputation of one or more toes | Amputation of foot | Amputation of shank | Amputation of thigh |
|-----------|--------------------------------|-----------------------------------|-----------------------|------------------------|------------------------|
| Sex | | | | | |
| Male | 29 | 32 | 15 | 5 | 33 |
| Female | 13 | 15 | 3 | 2 | 12 |

as age, waist measurement, family history, medical history of cardiovascular diseases and gestational diabetes (in women).

2. Once they are identified, individuals at a higher risk for type 2 diabetes should be tested to check their blood glucose level to diagnose pre-diabetic conditions, such as impaired fasting glycaemia and/or impaired glucose tolerance. Preventive measures should be taken with respect to the patients diagnosed with those conditions with a view to reduce or delay in time the occurrence of type 2 diabetes.

3. Losing weight and doing regular physical exercises can help to delay the appearance of type 2 diabetes. Active walking for at least 30 minutes each day can reduce the risk by 35-40%. Swimming, cycling and dancing are also suitable.

Type 2 diabetes is common in at least 90% of all cases of hyperglycemia.^[21,22] It is manifested by insulin resistance (impaired ability of the body to utilize efficiently insulin) and relative insulin deficiency, while one or both of these disorders are available as early as at the time of diagnosing hyperglycemia.^[21,22] Type 2 diabetes is typical in middle-age or advanced-age individuals (it is more common in people over 50 years old); however, it can also affect young overweight or obese individuals, as overweight and obesity may provoke insulin resistance.^[21,22] Type 2 diabetes may remain undiagnosed for months or even years (unidentified by medical specialists), whereas it is often found accidentally when measuring blood glucose or urine glucose, or when some of the complications caused by long-lasting hyperglycemia occur.^[21,22] Overweight and obesity, as well as lack of physical exercise on a regular basis may also cause insulin resistance and relative insulin deficiency, thereby, leading to a rise in blood glucose levels.^[21,22]

Both types of diabetes are major health deterioration conditions.^[22] There is no such thing as a mild form of diabetes. People suffering from diabetes are also at an increased risk of a number of major health problems.^[22] The permanently increased levels of blood glucose may provoke the appearance of galloping vascular-degenerative syndrome, affecting mainly the vessels of heart, eyes, kidneys and limbs.^[22] In addition, hyperglycemia leads to an increased risk and appearance of infections.^[22] The control of blood glucose, arterial pressure, and cholesterol aimed at maintaining levels which are close to the normal values in individuals of good health may help to suspend or delay the occurrence of diabetes complications. Therefore, regular measurements of these parameters is essential in diabetic patients.

Convincing evidence is available which changes the lifestyle (achieving a healthy body weight and moderate physical activity) may also help to prevent or delay the development of type 2 diabetes. This is known as primary prevention of this disease. Obesity, particularly in the abdomen area (large waist measurement), is linked to the appearance of type 2 diabetes. The loss of fats in the abdomen area improves insulin resistance and facilitates the control of metabolic deviations.^[20-22] Therefore, obese individuals should be encouraged to achieve and maintain a body weight within the specified healthy limits. Regular physical activity is one of the key components of primary prevention; moderate motion activity helps to maintain a healthy body weight, reduces blood pressure, reduces resting heart rate, increases muscles insulin sensitivity, contributes to weight loss in obese patients (facilitates burning of body fats).^[20-22]

A well-balanced nutritious diet is essential for a good health. A healthy diet may help to reduce the risk of cardiovascular diseases.

Other factors which influence the metabolism are as follows:

1. Smoking: an identified risk factor for a number of chronic diseases, including type 2 diabetes and related complications.^[23] Regular smoking leads to increased abdominal fat accumulation and insulin resistance. All smokers should be encouraged to cease smoking. Nevertheless, smoking cessation often leads to weight gain, unless measures to reduce nicotine-addiction symptoms are taken (mainly eating extra carbohydrates-containing snacks).

2. Stress and depression: Evidence is available on the relation between stress and depression and the increased incidence of diabetes and cardiovascular diseases.^[24] Most probably, at least in some people, it is due to an unhealthy diet (eating of unhealthy and highly caloric foods, smoking, and lack of exercise). People suffering from depression tend to neglect the health concerns.

3. Sleeping: Both chronic lack of sleep (shorter than six hours) and excess sleep (longer than nine hours) are associated with increased risk of type 2 diabetes.^[25] Insufficient sleep may induce hormonal alterations which control appetite (food acceptance) and energy consumption. The impaired balance between them leads to weight gain. Excess sleep may be also a sign of sleeping apnea or depression. Between obesity and snoring (obstructive sleeping apnea) most common sleeping disorder, there is also a well-established

association.^[25] People with type 2 diabetes suffer more often both from depression and obstructive sleeping apnea than the healthy population.^[25]

Furthermore, it is of utmost importance to take preventive measures for the development of diabetic foot, a complication of the disease. The followings must be strictly adhered: daily foot hygiene, disinfection with a 20 mg/L colloid silver solution, drying and airing the spaces between toes, in the case of dry skin-usage of suitable creams, etc.^[9,11,15] The choice of footwear is also essential-diabetic patients most often suffer from fallen arches of foot (symptomatic flat feet). Footwears with orthopedic soles are very suitable, and if not available, shoe insoles can be used. Preferably, shoes made of leather or with breathing membrane should be worn to prevent foot sweating-a basic factor predisposing the occurrence of fungal infections.^[9,11] Shoes must be periodically disinfected and checked inside for the presence of uneven areas, small stones, and projecting nails. These seemingly negligible agents can seriously damage the foot, which is likely to be less sensitive due to polyneuropathy. The socks should be also made of natural fabrics-cotton, they should be dry and clean, and they should be changed daily. In case of severe foot deformities, it is necessary to use tailored orthopedic footwears.

In conclusion, based on the findings of this review, the following conclusions and recommendations can be suggested: (i) diabetic foot is a major social disease; (ii) diabetic foot should be treated as a separate complex of symptoms, and not as a diabetic complication; (iii) early diagnostics, timely treatment, and proper prophylaxis are the key factors preventing complications and ensuring good quality of life of diabetic patients.

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